Elementary
LABORATORY EXPERIMENTS IN ORGANIC CHEMISTRY

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LABORATORY EXPERIMENTS
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Elementary
LABORATORY EXPERIMENTS
in ORGANIC CHEMISTRY

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THIRD EDITION

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PREFACE TO THE FIRST EDITION

This laboratory manual is designed for beginning students in organic chemistry whether they are specializing in chemistry or are merely seeking a knowledge of the subject for use in medicine, agriculture, home economics, biology or related fields.

The authors believe that it is very desirable for the beginning student to acquire an understanding of the more important manipulations and procedures in the organic chemical laboratory before any attempt is made to prepare organic compounds or study organic chemical reactions. As a consequence a number of preliminary experiments have been set apart to be carried out first and are designed to give an opportunity to teach the student not only technic but also the important principles involved in the common laboratory procedures. This gives the student laboratory work while the introductory part of the theoretical considerations is being covered in the lectures, and at the same time makes it possible for the student later to devote all his time and energy to a better understanding of the reactions involved in the experiments.

Opinions differ as to whether or not beginning students should be offered numerous test-tube experiments covering an extensive number of reactions, or should be offered comparatively few experiments carried out so that the products are isolated and purified. The authors feel the latter plan is distinctly the more instructive and interesting to the student, and it is the one followed in this manual.

The choice of experiments has been made to include the following types of preparations: (1) those representing some of the more important reactions, (2) those involving the preparation of substances readily obtained in good yields, (3) those using the cheapest reagents coincident with the best results, (4) those presenting series of reactions so that a student may use previously prepared materials, such as the series—nitrobenzene—analine—acetanilide—*p*-bromoacetanilide, etc. In a number of cases two or three experiments involving the same type reaction are included, so that all of the students in a class need not necessarily do the same experiment to illustrate the same general reaction. This duplication of type experiments serves the further purpose of emphasizing to the student the fact that each of such experiments merely represents a specific example of a general reaction. Moreover, a certain variation which may be desired from one year to another is thus made possible.

Particular care has been taken to describe each experiment in great detail even to specifying the amount of washing or drying reagent to be used in each instance and the exact strength of any reagents used which do not appear on the side-shelf. This has not been the practice in previous manuals and the criticism may be offered that the present method may lead the student to too much of a routine point of view. There are so many details to be learned, however, in beginning the study of organic chemistry, that the procedure suggested is believed to be the better one, particularly if the experiments are accompanied by questions concerning the principles involved. The student is then prepared in the second semester to undertake experiments where such details are not included and is able to use the proper judgment in setting up apparatus and in the use of reagents.

The questions at the end of each experiment are designed to determine whether the student understands the principles and the significance of the experiment performed. Such questions form an important part of the laboratory instruction. The teacher must designate to the class whether part or all of the questions must be answered, since this will depend upon the extent of the theoretical organic chemistry which has been presented.

The order and number of experiments to be carried out must be determined by the individual teacher for any particular class in organic chemistry. The experiments must necessarily be accompanied by occasional demonstrations and lectures covering general instructions and discussions of the various reactions. In order to indicate the amount of work that may be expected, but in no way to attempt to select the best experiments to be chosen, a few outlines of courses are given.[1] Other experiments have been included suitable for any superior students who have extra time.

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[1] The outlines given in the earlier editions have been modified to include the new experiments and are now placed in the appendix (page 395) along with other material of interest to the teacher.

A convenient and successful procedure for keeping notes and determining a student's ability is described. This happens to be the one used at the University of Illinois and at Cornell University laboratories, but there are many other methods which may be preferable in meeting other conditions. The pages of the manual have been perforated so that, if desired, the experiment sheet may be removed and attached directly into the notebook.

The introductory chapters attempt to explain merely the more important facts and theories concerning the general procedures in organic chemistry. It is better for the beginning student to get just the facts which he can remember and use, and to acquire more and more details later as he becomes advanced. This principle differs from many of the texts in which so many details about various procedures are given that the student does not learn them all readily.

For the convenience of the student, the strength of all the reagents commonly used on the side-shelf and the precautions in the use of certain materials are included. For the aid of the teacher the amounts of chemicals necessary for ten students for each experiment are listed, though no mention is made of the amount of reagents which commonly appear on the student's desk, such as dilute acids and alkalies and the common concentrated acids. The time required by an average student for each experiment is also given, with an indication of the period devoted to refluxing or standing, during which time the student may be working on other experiments. As the beginning student is usually unfamiliar with the common apparatus used in organic chemistry a page of diagrams is inserted. A graphic description of the method for making a fluted filter and a copy of a convenient card upon which the student may report his experiments are included.

Certain special solutions such as ammoniacal cuprous chloride, ammoniacal silver nitrate, Fehling's solution, or phenylhydrazine reagent, are described under the particular experiments in which they are to be used, and each student is expected to prepare them, or to be familiar with the method of preparation of such solutions.

The authors wish to acknowledge here their indebtedness for suggestions and advice given by Drs. James B. Conant, C. S. Marvel, H. T. Clarke, W. H. Carothers, and others, for aid in assembling the manual by Letha A. Davies, and for the help obtained from *Organic Syntheses* and a few of the other outstanding laboratory manuals in organic chemistry.

R. A.
J. R. J.

August, 1928.

PREFACE TO THE SECOND EDITION

The revision of the first edition of this manual has made possible the inclusion of sixteen additional experiments: urea from ammonium cyanate, *m*-bromotoluene, hydrazobenzene, distillation under diminished pressure, benzyl alcohol and benzoic acid, benzalacetophenone, benzoin and benzil, benzilic acid, diphenylacetic acid, cinnamic acid, *β*-bromostyrene, ethyl *n*-butylacetoacetate, methyl *n*-amyl ketone, ethyl *n*-butylmalonate, *n*-caproic acid, quinoline. This expansion has been made in response to many requests for sufficient material for a full year's course.

The same policy has been followed as in the preparation of the first edition. Experiments have been selected to illustrate important reactions and, where possible, to involve a sequence of preparations (such as *p*-acetotoluidide—bromoacetotoluidide—bromotoluidine—*m*-bromotoluene, or benzoin—benzilic acid—diphenylacetic acid). Preference has been given to experiments in which the products are obtained in good yields and in which comparatively inexpensive chemicals are used. In this edition there has been added a list of suggestions for additional preparations appearing in well-known manuals (with references). This is intended for students who are qualified for further synthetic work.

With a view to economy of reagents, the quantities of the starting materials have been reduced (about one-half or one-third) in several experiments. This policy has not been carried to an extreme as the authors feel that the manipulation of small quantities of materials should not be stressed in an elementary course.

The authors wish to acknowledge the help obtained from *Organic Syntheses* and from Gattermann-Wieland, *Laboratory Methods of Organic Chemistry*. The authors are grateful for advice and suggestions given them by many teachers of organic chemistry, particularly Drs. L. F. Fieser, R. C. Fuson, C. D. Hurd, R. J. Kaufman, R. L. Shriner, and E. A. Vuilleumier.

R. A.
J. R. J.

JANUARY, 1933.

PREFACE TO THE THIRD EDITION

Since the appearance of the second edition of this manual the progress in synthetic organic chemistry has been very extensive and it now seems desirable to include in the work of the elementary student, many types of experiments which have previously been limited to advanced students. To illustrate certain of the important advances, new experiments have been added in the field of synthetic polymers and polymerization, in which such significant commercial developments have occurred during the last few years. The addition type of polymer is illustrated by the depolymerization of methyl methacrylate polymer ("Lucite") to the monomer, and polymerization of the monomer under the influence of a peroxide catalyst (p. 377). Condensation polymerization is illustrated by the preparation of a glyptal type of synthetic resin, many of which resins are so important as the bases of lacquers, varnishes and finishes (p. 375).

The general interest in the field of synthetic drugs has led us to include the preparation of aspirin (p. 357) and sulfanilamide (p. 359). The latter is an excellent sequence of reactions, and the product is of particular interest as it represents one of the most striking advances in chemotherapy of the last twenty years.

Other new experiments include the following: Cyclohexene from cyclohexanol, which gives a product that can be handled more conveniently than ethylene or amylene, and involves the use of an important alicyclic compound; *sec* or *tert*-Butyl Chloride from the alcohol, a short experiment illustrating the formation of alkyl chlorides; Cyclohexanone from cyclohexanol, representing the oxidation of a secondary alcohol to a ketone; Fumaric Acid from furfural, involving the use of an interesting heterocyclic compound and illustrating the use of an extremely important oxidation catalyst, vanadium pentoxide.

The new experiments have been chosen carefully not only with a view to broadening the scope of reactions covered, but with attention to the use of relatively inexpensive and readily available materials.

Several of the introductory sections dealing with typical laboratory operations and technic have been revised and expanded. In a number of the preparations brief discussions have been added to direct attention to theoretical and practical points, and to recent technical developments. Minor improvements have been introduced in various procedures, based upon the experience of various groups of students in the laboratory. A number of test reactions and procedures for identification have been added. These small-scale tests, where a crystalline product is actually isolated, serve admirably to illustrate an important phase of organic laboratory work. Furthermore, if the laboratory time is limited severely, such experiments permit the student to cover a larger field than could be done with the ordinary larger scale preparations.

Several new figures have been added to illustrate the discussions of melting-points and of fractional distillation. Directions are given for the construction of an inexpensive air-driven stirrer which has given excellent service in the elementary laboratory. Diagrams of this stirrer and of a typical stirring assembly have been included. The authors are indebted to Dr. W. T. Miller for the design of the stirrer.

The authors will be glad to receive from other teachers comments and criticisms or suggestions concerning the material in the manual. Grateful acknowledgment is made for the help in this revision from many instructors in organic chemistry, especially Drs. W. F. Bruce, J. A. Geissman, W. T. Miller, R. L. Shriner, and H. B. Snyder.

R. A.
J. R. J.

MARCH, 1940.

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Experiments
On Laboratory Operations

INTRODUCTION

Foreword

The fundamental aim of laboratory work in elementary organic chemistry is to teach the methods which are used in this field and to acquaint the student with the most common organic materials. A student should get first-hand experience of the fact that organic chemistry deals not only with formulas and names but with substances having definite, distinct, and characteristic properties. The student should learn especially to regard the preparation of any specific compound by a general method not only as a means of preparing this specific compound but also as an illustration of a general method applicable to an entire class of compounds.

Two factors which contribute to excellence in laboratory work are accuracy and neatness. Accuracy involves performing of experiments in a careful manner and in accordance with the laboratory directions, making careful observations and drawing logical conclusions, and thoroughly understanding the experiment. Promptness in recording experimental observations in the notebook is necessary for accuracy. Neatness applies to the manipulation of reagents and apparatus, the cleanness of equipment, and the appearance of the notebook.

Although each student is required to perform a certain number of experiments, the object is not the mere mechanical performance of experiments or the preparation of a few organic compounds, but is to acquire a knowledge of the basic principles involved.

Laboratory Notes[1]

In order to do good laboratory work, it is essential to have a suitable notebook in which to record directly the observations made during experiments, and in which to assemble information which will aid in the performance of the experiment. For this purpose the student should procure a stiff-covered *bound* notebook, about 8 × 10 inches, provided preferably with cross-sectioned paper (for facilitating the preparation of tables of physical constants which are required in the later experiments). The use of loose-leaf notebooks for laboratory records is not satisfactory, and the recording of experimental observations on loose sheets or scraps of paper is not permissible. It is preferable to record notes in ink, and if corrections are necessary these should be made by additional notes rather than by erasures.

---

[1] The following specific directions for the preparation of notebooks and the general laboratory procedure are those which are used in the elementary courses in organic chemistry at the University of Illinois and at Cornell University. For the particular conditions which obtain in other laboratories, the instructor in charge of the laboratory work may wish to alter these directions or substitute others.

For the preliminary experiments the student is expected to proceed in the following way:

1. Read the descriptive paragraphs concerning the laboratory operation which is to be carried out (these are found immediately preceding each experiment).

2. Read the laboratory directions for the entire experiment, note particularly the cautions for handling materials, and consider the reasons for the procedure which is to be followed.

3. In the notebook, write a statement of the process which is to be carried out, and attach the laboratory direction sheet. All laboratory directions in the manual are on perforated sheets which can be detached and pasted in the notebook. In experiments where chemical tests are made, write equations for the reactions.

To gain time for laboratory work, the student should carry out the instructions in the above paragraphs before coming to the laboratory. The schedule of experiments will be announced beforehand, so that the student will have an opportunity to prepare his notebook and be ready to start laboratory work at the beginning of the laboratory period.

4. After completing the instructions in the above paragraphs, arrange the apparatus for the experiment and secure the approval of the laboratory instructor for the set-up.

5. Perform the experiment according to the laboratory directions and record observations directly in the notebook. When the experiment has been completed, dismantle the set-up and clean the glassware and apparatus at once.[1]

---

[1] It is advantageous to clean glassware and apparatus immediately, since it is usually easier to remove tarry and gummy substances while they are fresh. Furthermore, much time is saved by having the equipment always clean and ready for use.

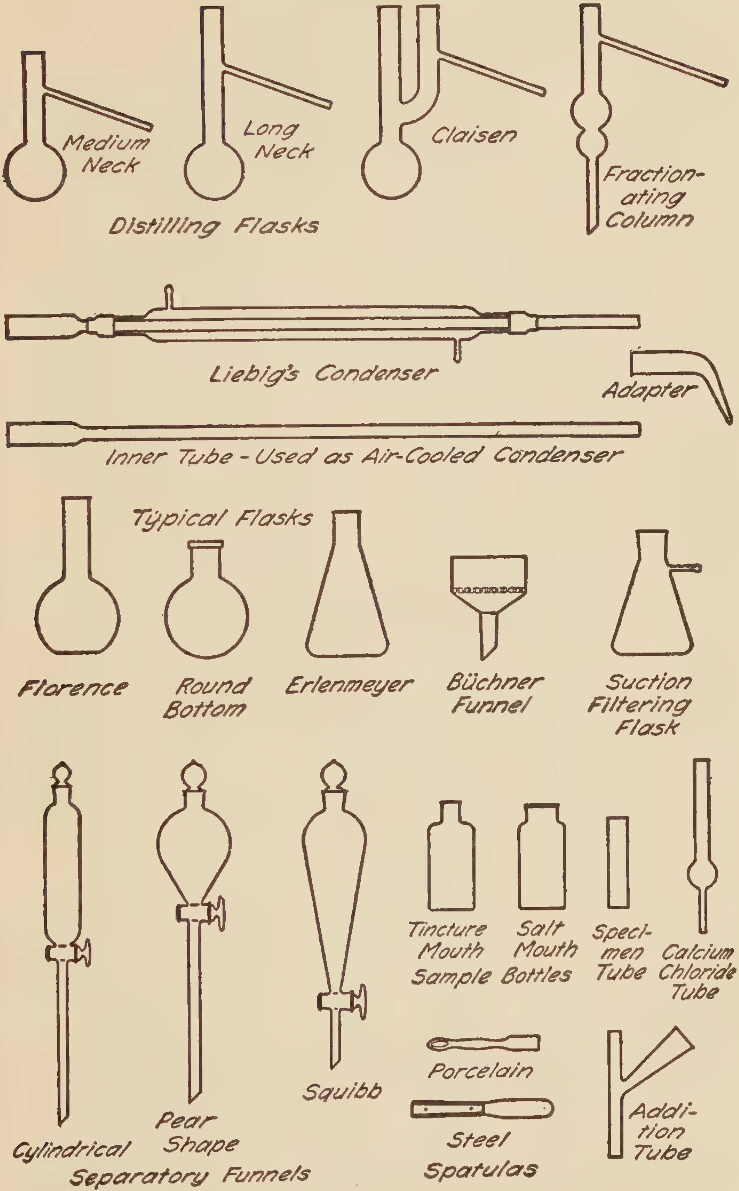
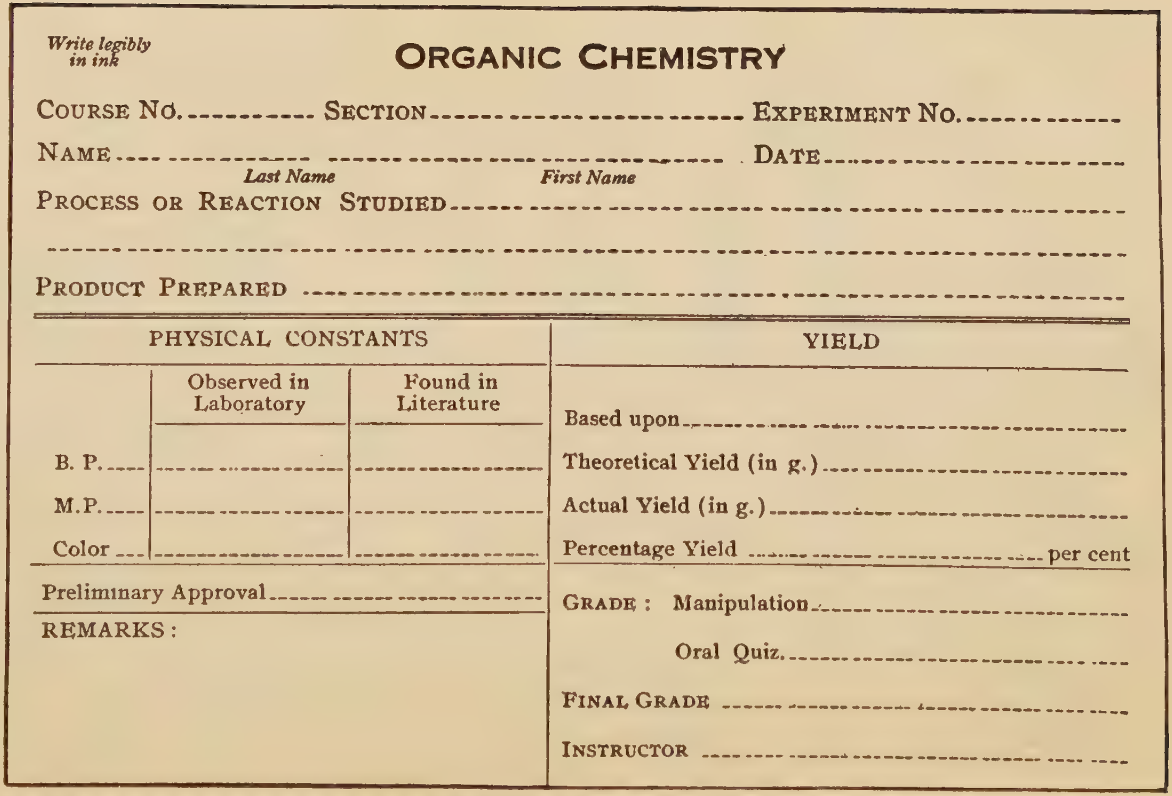


Fig. 1.—Common Organic Laboratory Apparatus.



Write legibly in ink

ORGANIC CHEMISTRY

COURSE NO. ---------- SECTION -------------------- EXPERIMENT NO. ------------

NAME ------------ ------------------------ DATE ----------------
Last Name *First Name*

PROCESS OR REACTION STUDIED --

PRODUCT PREPARED --

PHYSICAL CONSTANTS		
	Observed in Laboratory	Found in Literature
B. P. ----	----------------	----------------
M.P. ----	----------------	----------------
Color ---	----------------	----------------

Preliminary Approval --------------------

REMARKS:

YIELD

Based upon --

Theoretical Yield (in g.) ----------------------------

Actual Yield (in g.) --------------------------------

Percentage Yield ------------------------ per cent

GRADE: Manipulation ----------------------------

Oral Quiz. ----------------------------

FINAL GRADE ----------------------------------

INSTRUCTOR ----------------------------------

Sample Report Card
(Actual size 4 × 6 inches)

6. Draw conclusions from the results, and write answers to the questions given on the direction sheets. Make complete statements in answering the questions.

7. Submit the completed notes and the report card (see page 6), together with any substance prepared, to the laboratory instructor for approval, as soon as possible after the completion of the experiment. At this time the instructor will examine the notes and may ask questions pertaining to both the theoretical and practical parts of the experiment.

The grade for the experiment is based upon the student's neatness and skill in carrying out the experiment, and upon his knowledge of the underlying principles and generalizations. No credit is given for the performance of experiments if the notes are not submitted for approval.

NOTES ON REAGENTS

In performing laboratory experiments it is important to weigh or measure the amounts of materials carefully and to use the exact quantities which are called for in the directions. When reagents need not be accurately measured (as for certain tests), the laboratory directions indicate approximate quantities. When an approximate quantity is indicated, as 1–2 cc., the student should use a quantity within the specified limits. At first it will be advisable actually to measure the quantity used, in order to learn to judge such quantities, but after some experience the student should be able to estimate approximate quantities.

TABLE I

DESK REAGENTS

REAGENT	SP. G.	GRAMS OF REAGENT		MOLES PER LITER (APPROX.)
		Per 100 g.	Per 100 cc.	
Acetic Acid (glacial)	1.06	99.5 g.	105.5 g.	17.5
Hydrochloric Acid (concd.)	1.18	35.4 g.	42 g.	12
Hydrochloric Acid (dil.)	1.08	15 g.	17.5 g.	5
Nitric Acid (concd.)	1.42	70 g.	100 g.	17
Sulfuric Acid (concd.)	1.84	96 g.	176 g.	18
Sodium Hydroxide Solution (dil.)	1.11	10 g.	11.1 g.	3
Ammonia Solution (concd.)	0.90	29 g.	26 g.	15

It is never permissible to estimate or guess at quantities of starting materials which are to be used in carrying out a preparation. In many cases the success of an operation depends not only upon the starting materials but also upon the use of certain reagents in definite amounts. It is usually advantageous and sometimes absolutely necessary to know at least fairly accurately the amount of each reagent which is present. A careful laboratory worker will acquire the habit of using solutions of known strength, and of weighing or measuring the reagents and solutions used. The strengths of the most common laboratory reagents are listed above.

Interconversion of Weights and Volumes

In laboratory practice it is often necessary or desirable to convert weight measures into volume measures, and vice versa. These conversions may be made by use of the following relationships:

$$\underset{\text{(in g.)}}{\text{Weight}} = \underset{\text{(in cc.)}}{\text{Volume at } t^\circ} \times \underset{\text{(in g. per cc.)}}{\text{Density at } t^\circ}$$

$$\underset{\text{(in cc.)}}{\text{Volume at } t^\circ} = \frac{\text{Weight (in g.)}}{\text{Density at } t^\circ \text{ (in g. per cc.)}}$$

The numerical values of the density and the specific gravity of a particular liquid (at a given temperature) are usually so nearly equal that they may be used interchangeably for approximate calculations. Nevertheless, the student should bear in mind the following accurate definitions:

The density of a liquid is equal to the mass of a unit volume of the substance. An accurate density value includes a statement of the temperature and the units; for example, the density of water at 20° is 0.9982 g. per cc. Since the unit of mass (the gram) is equal to the mass of 1 cc. of water at 4°, the following notation is often used: $d_{4^\circ}^{20^\circ} = 0.9982$.

The specific gravity of a liquid is the ratio of the weight of any volume of the liquid to the weight of an equal volume of water *at some stated temperature.* If the specific gravity of a liquid at a temperature t° is referred to a volume of water at 4°, the specific gravity is numerically exactly equal to the density at t°. Often the specific gravity at a given temperature is determined with reference to water at a given temperature; the following notations may be used for such values: *sp. g.* $\frac{20^\circ}{20^\circ}$ or $d^{20^\circ}_{20^\circ}$. Obviously the latter values are not numerically equal to the density at 20°. The values may be interconverted by the following relationship:

$$\text{Density}\,\frac{t^\circ}{4^\circ} = \text{Spec. grav.}\,\frac{t^\circ}{t^\circ} \times \text{Density of water}\,\frac{t^\circ}{4^\circ}.$$

When aqueous solutions are used, or substances containing water, such as concd. hydrochloric acid, concd. sulfuric acid, 95 per cent alcohol, etc., it is necessary to calculate the weight of solute which is present.

$$\underset{\text{(in g.)}}{\text{Weight of solute}} = \underset{\text{(in g.)}}{\text{Weight of solution}} \times \text{g. of solute per g. of the solution}$$

$$= \underset{\text{(in g.)}}{\text{Weight of solution}} \times \frac{\text{per cent of solute by weight}}{100}.$$

For the sake of convenience, the physical constants of solutions of the common acids and of ethyl alcohol are included in the appendix (page 390). More complete tables may be found in the chemical handbooks and in reference works.

The use of these physical constants is shown by the following example. Let us suppose that we wish to find the weight of pure ethyl alcohol which is present in 30 cc. of ordinary ethyl alcohol (95 per cent by volume, or 92.5 per cent by weight). By reference to an "alcohol table," the density of 92.5 per cent (by weight) ethyl alcohol at 20° is found to be 0.8112 ($d^{20^\circ}_{4^\circ}$). Using the equations above:

Weight of 30 cc. of 92.5 per cent alcohol

$$= 30 \text{ cc.} \times 0.8112 \text{ g. per cc.} = 24.34 \text{ g.}$$

$$\text{Weight of pure ethyl alcohol (100 per cent)} = 24.34 \text{ g.} \times \frac{92.5}{100} = 22.5 \text{ g.}$$

These two calculations may be made in a single operation:

Weight of pure ethyl alcohol

$$= 30 \text{ cc.} \times 0.8112 \text{ g. per cc.} \times \frac{92.5}{100} = 22.5 \text{ g.}$$

The general statement of the equation is the following:

Weight of the pure solute

$$= \underset{\text{(in cc.)}}{\text{Volume at } t^\circ} \times \underset{(d^{t}_{4^\circ}\text{ in g. per cc.})}{\text{Density of the solution}} \times \underset{\text{(by weight)}}{\text{Concentration.}}$$

PURIFICATION OF COMPOUNDS

Since organic compounds do not usually occur in a pure condition in nature, or are accompanied by impurities when synthesized, the purification of materials forms an important part of laboratory work in organic chemistry. For this purpose, three general procedures are available: distillation, crystallization, and extraction. The process used in any particular case depends upon the characteristics of the substance to be purified and the impurities to be removed.

The purpose of the preliminary experiments is to familiarize the student with these fundamental processes, so that in the preparations which follow, the student will be able to work more efficiently. For this reason, it is important to carry out the preliminary experiments with the idea of learning the correct methods of manipulation.

Physical Constants

A pure compound (a homogeneous chemical individual) possesses certain physical properties which are distinguishing characteristics of the compound in question. The characteristic physical constants are common to all samples of a given compound, provided that the samples exist under the same external conditions.

In order to test the purity of organic substances, the characteristic physical constants are determined, and if possible compared with those of the pure substances as reported in the chemical literature. The physical constants most commonly used are:

melting-point (for solids),
boiling-point under a known pressure (for liquids or low-melting solids),
density at a stated temperature (for liquids),
refractive index (usually applied only to liquids), at a stated temperature, for light of a specified wave-length.

Other physical constants are solubility in various solvents, molecular weight, surface tension, dielectric constant, and optical rotation. Of all physical constants melting-point and boiling-point are used most frequently.

MELTING-POINTS

The true melting-point of a crystalline substance is defined as the temperature at which the solid phase exists in equilibrium with the liquid phase. On account of the relatively large samples which are required for such determinations, the melting-points which are usually observed in the organic laboratory (as well as most of the melting-points recorded in handbooks and in the chemical literature) are not true but capillary melting-points. These values are comparable among themselves but are usually slightly higher than true melting-points.

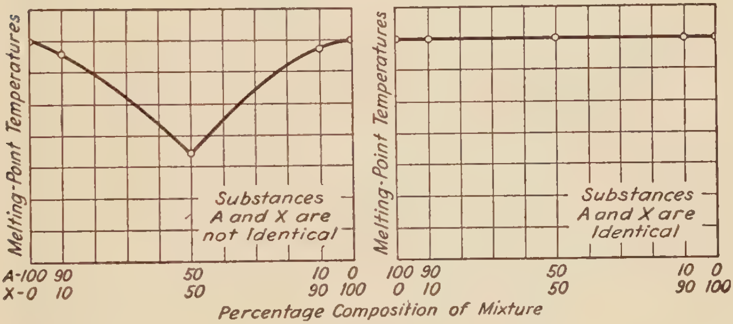
For the determination of the melting-point a small amount of the finely-powdered crystals is introduced into a capillary tube, which is fastened to a thermometer, and the tube and thermometer are heated in a bath, usually of cottonseed or paraffin oil. The temperatures recorded as the observed melting-point are the temperatures at which the substance commences to liquefy and that at which it becomes completely liquefied. The melting-point range (the interval between the beginning of liquefaction and complete liquefaction) and the actual temperature of the melting-point are valuable indications of the purity of the substance.

Pure crystalline organic substances usually possess a sharp melting-point, that is, the melting-point range is very short (0.5–1.0°). The presence of even small amounts of miscible, or at least partially miscible, impurities will usually produce a marked increase in the melting-point range, and a depression of the actual temperature of the melting-point. These facts are made use of in establishing the identity of organic compounds by the method of "mixed melting-points," as shown below.

A sharp melting-point is usually an indication of high purity of a crystalline substance, but it is not necessarily so. Certain mixtures of organic substances, particularly of homologues and of isomers, possess rather sharp melting-points which remain practically constant after repeated crystallizations from a solvent. A more reliable indication is obtained by fractional crystallization from two or more widely different types of solvents, and determination of the melting-points of the various fractions. In the case of a pure compound, the melting-points of all of the fractions will be the same.

Mixed Melting-Points

Suppose that a substance to be identified, X, is suspected to be identical with one of two known substances, A or B, and that the three pure substances, A and B and X, have approximately the same melting-point. Let us then prepare mixtures of about equal amounts of A and X, and of B and X, and determine the melting-points of these mixtures. If A and X are different, the melting-point of the mixture of A and X will usually be lower than the melting-point of either A or X. If A and X are identical, the melting-point of the mixture will be the same as that of A and of X. The same reasoning is applied to the behavior of the mixture of B and X.

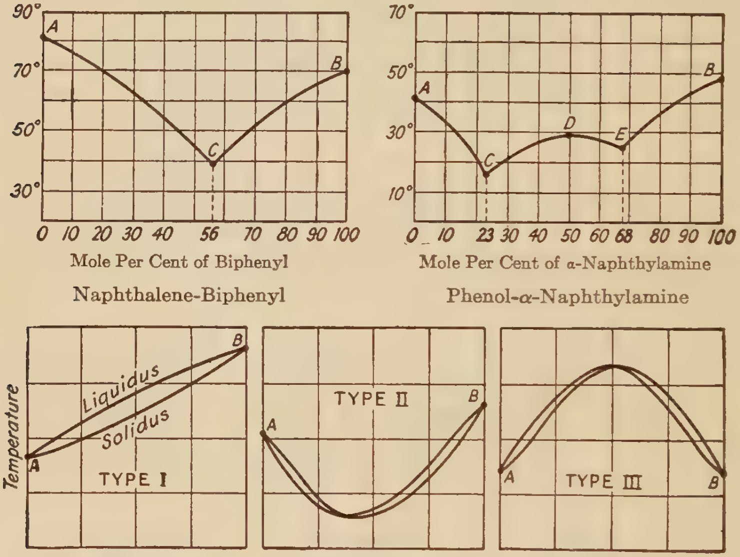


If the melting-points of the mixtures of A and X, and of B and X, are both below the original melting-points of the pure substances, then one must conclude that X is not identical with either A or B.

In practice it is often advisable to prepare a number of mixtures which contain varying proportions of the substances to be identified and the known substance; for example, a mixture containing 10 per cent of A and 90 per cent of X, another containing 50 per cent of each, and a third mixture containing 90 per cent of A and 10 per cent of X. The results of the melting-point determinations of these mixtures may then be plotted and a rough melting-point curve may be drawn. For this purpose the temperature plotted is that at which the mixture liquefies completely. The nature of the melting-point curves which are thus obtained is shown in the accompanying figures.

Actually, the melting-points of only three mixtures would not give sufficient data to reveal the details of the whole curve. Complete melting-point curves (also called freezing-point diagrams) of binary mixtures illustrating the varied types of curve that may be encountered in practice are shown in the figures on the following page.

Formation of Eutectic Mixtures. The behavior of naphthalene-biphenyl mixtures is typical of many organic compounds. The two components form practically "ideal" solutions over the entire range (*i.e.*, the freezing-point lowering is proportional to the mole-fraction of the solute present). The curve *A–C* shows the lowering of the melting-point of naphthalene (*A*, m.p. 80°) by admixture with biphenyl, and *B–C* the lowering of the melting-point of biphenyl (*B*, m.p. 69°) by naphthalene. The intersection *C* is a eutectic point (39.4°) at which temperature *both* crystalline solids *A* and *B* can exist in equilibrium with a melt of fixed composition (40% naphthalene + 60% biphenyl, by weight).



Naphthalene-Biphenyl

Phenol-α-Naphthylamine

Solid Solutions (No Maximum or Minimum)

Solid Solutions (With Minimum)

Solid Solutions (With Maximum)

Fig. 2.—Melting-Point Curves.

The phenol-α-naphthylamine curve illustrates a case in which the components *A* and *B* form a compound, of the composition *AB*. The addition of α-naphthylamine to phenol (*A*, m.p. 41°) lowers the melting-point until the point *C* is reached; further addition then raises the melting-point until *D* is reached. A similar phenomenon occurs upon addition of phenol to α-naphthylamine (*B*, m.p. 49°) until the point *D* is reached. This indicates the formation of a compound of the composition *AB* (m.p. 28.4°). Point *C* represents a eutectic of *A* and the compound *AB*, and point *E* a eutectic of *B* and the compound *AB*. It should be noted that the point *D* (m.p. of the compound formed) may be higher than *A* or *B*. The abscissa of *D* gives the composition of the compound formed; occasionally several compounds of A and B are formed, having different compositions (A_2B, AB, AB_2, etc.).

Formation of Solid Solutions. In the preceding examples the individual components (A or B or AB) form separate crystals in solidifying from the melt. In other cases a homogeneous solid solution ("mixed crystals") of A and B (or A and AB, etc.) is formed. Three different types of curve are known for solid solutions, when the components are miscible in all proportions. Each of these diagrams is made up of two parts, one for the composition of the liquid solutions (liquidus curve) and another for the solid solutions (solidus).

In one type all mixtures of A and B melt at temperatures intermediate between the melting-points of pure A and pure B, and there is neither a minimum nor maximum in the curve (Type I, Fig. 2). This situation illustrates a case where the melting-point of pure A is *raised* by admixture with B, but that of pure B is lowered by addition of A. The second type of curve (Type II, Fig. 2) has a minimum, and the melting-point of either A or B is lowered by admixture with the other. The third type of curve (Type III, Fig. 2) passes through a maximum, and here the melting-point of either A or B is *raised* by adding the other to it. This unusual form of curve is encountered occasionally with mixtures of optical isomers.

Experiment 1

DETERMINATION OF MELTING-POINTS

Arrange a melting-point bath in the following way: Prepare a stirring rod, bent so as just to fit into a 100–150-cc. beaker, and provided with a long handle which serves for moving up and down. Place the beaker on an asbestos-centered wire-gauze supported on a ring fastened to an iron stand. With a cork-borer of the proper size, drill one hole in a 20–25 mm. cork and insert a thermometer.

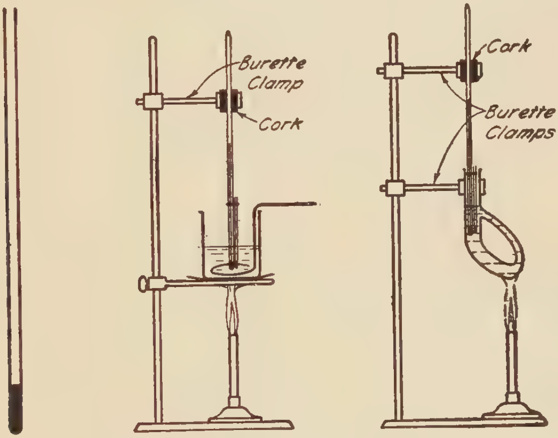


Fig. 3.—Melting-Point Apparatus.

Support the cork in a burette clamp so that the thermometer is held vertically in the center of the beaker, with the mercury bulb about 1 cm. above the bottom of the beaker. When the apparatus is properly arranged, fill the beaker *not more than two-thirds full* of cottonseed oil (see Fig. 3).[1] A larger amount of bath liquid should not be used as the oil expands on heating and will overflow or spatter during a melting-point determination.

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[1] Other suitable bath liquids, for temperatures up to 250–275°, are: medicinal paraffin oil ("Nujol," etc.), olive oil, *n*-butyl phthalate, "arochlor" #1242 (technical mixtures of chlorinated biphenyl).

Prepare a number of small capillary tubes (often called melting-point tubes) in the following way: Heat a test-tube, or other glass tube of large diameter, in a hot flame until thoroughly softened, remove from the flame and draw out until the outside diameter of the tube is about 1–2 mm. Break this fine tube into lengths of 8–10 cm. by means of file marks and seal one end by just touching at the edge of a flame.

Take a small amount (0.1–0.2 g.) of the substance of which the melting-point is to be determined, and finely pulverize with a spatula or clean knife-blade on a small fragment of clay plate or on a piece of smooth paper. Make a little mound of the pulverized material and thrust the open end of the capillary tube into it. Shake the solid down into the end of the tube by gently drawing a triangular file along the upper portion of the tube and then tapping the lower end of the tube on the desk-top. Repeat this procedure until the tube is filled to a height of 6–8 mm. and tap the tube vigorously several times to pack the solid tightly into the end of the tube. By means of a thin ring of rubber tubing, attach the capillary tube to the thermometer so that the solid is placed just alongside the mercury bulb.

Heat the oil-bath slowly with a small flame on an asbestos-centered wire-gauze, and stir with the stirring rod to obtain a uniform temperature rise. Heat fairly rapidly until the temperature rises to within about 12–15° of the melting-point (roughly determined in a preliminary trial) and then with a very small flame so that the temperature rises *regularly* at a rate between 2° per minute and 3° per minute. Continue to stir the oil throughout the heating and carefully observe the substance in the tube. Report as the observed melting-point the temperature at which the substance starts to liquefy and the temperature at which the melt is clear.

Another convenient form of melting-point apparatus is that devised by Thiele which avoids mechanical agitation. In Fig. 3 is shown a diagram of this apparatus as modified by Dennis. The principle involved is merely that the sulfuric acid usually used in the apparatus circulates due to heating. The temperature of the acid at the upper entrance from the main tube is higher by about 1.5° C. than at the lower exit, provided the acid is heated slowly.

(A) In a melting-point apparatus, determine the melting-point of urea, and of cinnamic acid, by the procedure outlined.

(B) Prepare a mixture of about 90 per cent urea and 10 per cent cinnamic acid by mixing together nine parts of urea and one part of cinnamic acid. For the purpose of this experiment, it is sufficient to judge the amount very roughly by the relative sizes of long thin piles of the powdered crystals. Mix the substances thoroughly on a small piece of smooth paper or fragment of clay plate, and determine the melting-point of the mixture.

(C) In the same manner prepare a mixture of about 90 per cent cinnamic acid and 10 per cent urea, mix thoroughly, and determine the melting-point of the mixture.

(D) In the same manner prepare a mixture of about equal quantities of urea and cinnamic acid, mix thoroughly, and determine the melting-point of the mixture.

(E) From the results obtained in the preceding paragraphs, plot a rough diagram of the melting-point curve of mixtures of urea and cinnamic acid. For this purpose the temperature taken as ordinate is that at which the mixture liquefies completely.

QUESTIONS

1. Define accurately the term melting-point.

2. What general conclusions can be drawn from these mixed melting-point determinations?

3. Suppose that two different organic compounds, *M* and *N*, have about the same melting-point, and that you are given an unknown organic compound, *X*, which also has the same melting-point and is suspected to be identical with either *M* or *N*. Describe your procedure and the results you would obtain, in each of the following situations: *X* is identical with *M*; *X* is identical with *N*; *X* is not identical with either *M* or *N*.

CRYSTALLIZATION

In a typical laboratory preparation, a crystalline solid in separating from the reaction mixture is usually contaminated with small amounts of impurities. The purification of such crystalline substances is usually effected by crystallization from a suitable solvent. The procedure consists essentially of three steps: (a) dissolving the substance in the solvent at a relatively high temperature, (b) causing the dissolved substance to crystallize from the solution by cooling to a low temperature, (c) separating the purified crystals from the supernatant solution (the mother-liquor).

The selection of a suitable solvent for crystallization is of great practical importance. The fundamental requirements of the solvent are: (a) it must not react in any way with the substance to be purified, (b) it must dissolve a moderate quantity of the substance at a high temperature and only a small quantity at a low temperature, (c) it should dissolve the impurities readily, (d) it must be capable of easy removal from the crystals of the purified substance. A number of other considerations such as ease of manipulation, cost, inflammability, etc., will also enter into the selection.

Table II

COMMON SOLVENTS FOR CRYSTALLIZATION

Solvent	B.P., Deg. C.	Solvent	B.P., Deg. C.
Water	100	*Carbon Disulfide	46
*Methyl Alcohol	64	*Acetone	56
*Ethyl Alcohol	78	Chloroform	61
*Butyl Alcohol	117	Carbon Tetrachloride	76
*Ethyl Ether	34	*Benzene	80
*Ethyl Acetate	78	*Petroleum Ether	50–90
*Acetic Acid (glacial)	119	*Ligroin	90–150

* Inflammable.

In selecting a solvent for the purification of a particular substance one must consider its effectiveness for removal of the following general categories of impurities:

Mechanical impurities, consisting of dust, particles of dirt, grit, etc., are readily removed by filtering the hot solution since they are practically insoluble in all of the common solvents. Admixed inorganic salts may often be separated in this way by using a solvent in which they are insoluble; an alternative method is to use a solvent, especially water, in which many inorganic salts are soluble and the organic compounds are insoluble.

Traces of coloring matter and resinous impurities may often be removed by warming the solution with *a small amount* of decolorizing charcoal or infusorial earth (Norite, Darco, boneblack, etc.) and filtering the hot solution. An excessive amount of decolorizing agent must be avoided since it will frequently adsorb the compound which is being purified.

Impurities less soluble in the solvent are very difficult to remove if they are present in considerable amount since only a small quantity will be held in solution by the mother-liquor.

Impurities of about the same solubility in the solvent, when present in moderately small amounts, are easily removed since they remain in solution in the mother-liquor.

Impurities more soluble in the solvent may often be almost completely removed by a preliminary washing of the crystals (see Extraction) with the cold solvent. The remaining traces may then be removed by crystallization since they are retained in the mother-liquor.

In many instances information is available concerning the solvents suitable for crystallization of the substance which is to be purified. If such information is lacking, the common solvents may be tested experimentally on a small scale in order to select a satisfactory one. Often a mixture of two solvents is more satisfactory than a pure solvent; such mixtures are usually made up of one solvent which dissolves the substance very sparingly, and a second solvent which dissolves the substance readily.

The size of the crystals of the purified product is also an important factor. With substances which crystallize readily, it is advisable to cool the hot solution rapidly with vigorous stirring, so that small uniform crystals are obtained. Small crystals usually occlude less of the impurities during crystallization and are more easily freed from the adhering mother-liquor. Not infrequently one may meet with a crystalline organic compound, particularly among low-melting substances, which will exhibit a marked tendency to separate from solution (even at temperatures well below the melting-point) in the form of an oily liquid which crystallizes with great difficulty. In such cases satisfactory crystallization may be obtained by cooling slowly and allowing the solution to stand for a considerable length of time. Occasionally it is necessary to prepare a dilute solution and to allow the solvent to evaporate slowly, but this practice should be used only as a last resort, since it is difficult to obtain a pure product in such a manner (Why?).

FILTRATION

Filtration is used for the separation of solid substances (often crystalline solids) from a liquid or solution in which they are suspended. The most important types of filtration encountered in the organic laboratory are: (1) Filtration for the purpose of removing mechanical impurities, or decolorizing agents, as in the purification of crystalline solids by crystallization from a solvent; (2) Filtration for the purpose of separating a crystalline solid from the mother-liquor in which it is suspended.

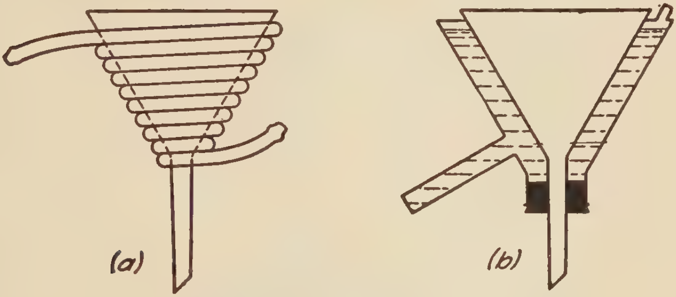
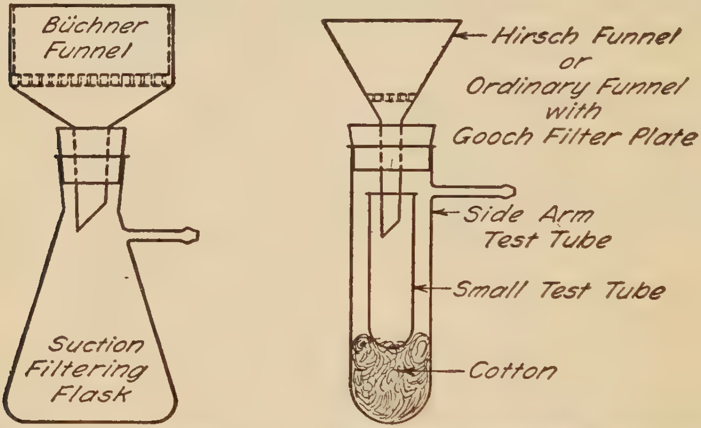


FIG. 4.—Funnels for Hot Filtration.

The first type of filtration is usually carried out at a relatively high temperature, in order to prevent the dissolved substance from crystallizing during the filtration. In order to avoid this inconvenience, a fluted filter paper (see Fig. 6) is used to obtain rapid filtration, and a large funnel with a short wide stem is employed to avoid separation of crystals and clogging in the stem. It is often advisable to warm the funnel gently over a small flame or in a jet of steam before filtration is started.

If a considerable quantity of the hot liquid is to be filtered, it is advantageous to warm the funnel externally during the filtration. For this purpose, two suitable devices may be employed: (a) a coil of small lead pipe, through which hot water or steam may be circulated, wound tightly around the funnel (see Fig. 4); (b) a metal jacket having a side-arm in which water or other suitable liquid may be heated (see Fig. 4).

For the separation of crystals from their mother-liquor, suction filtration is usually employed. This is carried out by placing the filter paper in a porcelain funnel provided with a fixed, flat, perforated plate (Büchner funnel) and using a suction filtering flask of heavy glass, with a side-tube for attachment to a suction pump (see Fig. 5). The use of suction makes possible a very rapid filtration and a more complete removal of the mother-liquor than would be possible otherwise. In using a Büchner funnel the filter paper should be selected (or trimmed if necessary) so that it lies perfectly flat upon the perforated plate and does not fold up against the sides. It is wise to use two thicknesses of filter paper, and to moisten the papers with the solvent before starting the filtration.



Ordinary Suction Filtration — Suction Filtration of Small Quantities

FIG. 5.—Apparatus for Suction Filtration.

To free the crystals from adhering mother-liquor, they are first pressed firmly upon the filter with a clean cork or spatula. The suction is then released and the crystalline cake loosened with a spatula. The washing liquid is added in small portions and the material is worked into a smooth paste. When this is accomplished the suction is applied again, and the crystals are pressed as before to remove the liquid as completely as possible. It is important in washing crystals to stop the suction and break up the crystalline cake so that the whole mass may actually come into contact with the washing liquid. Another very efficient way of removing the mother-liquor is by means of a centrifuge.

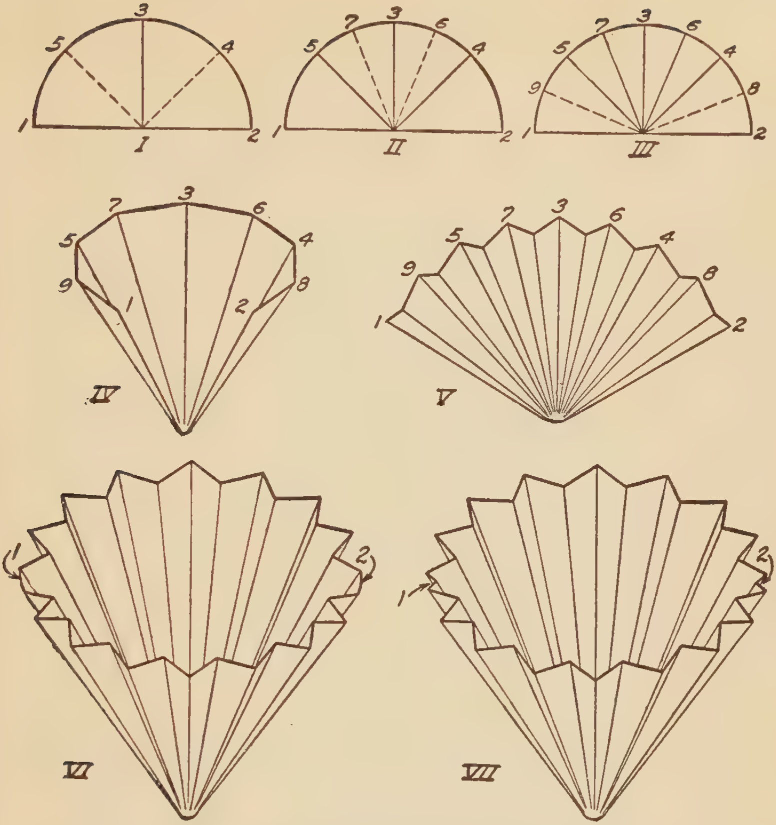


Fig. 6.—Preparation of a Fluted Filter.

Select a filter paper and glass funnel of such dimensions that the top of the folded paper is 5–10 mm. *below* the upper rim of the funnel (120 mm. diam. paper for a 65 mm. funnel, 185 mm. paper for a 100–120 mm. funnel, etc.). Fold the paper in half, and again into quarters (part I, Fig. 6). Bring each edge *into* the center fold and crease again, producing new folds at *4* and *5*. Do not crease the folds tightly at the center—this would weaken the central portion so that it might break during filtration. Continue the series of *inward* folds, bringing *2* into *5*, *1* into *4*, *2* into *4*, *1* into *9* (II and III, Fig. 6).

Grasp the folded filter cone (IV, Fig. 6) in the left hand and make a new fold in each segment, between *2* and *8*, *8* and *4*, etc., *in a direction opposite to the first series.* The result is a bellows or fan arrangement (V). Open the filter paper completely and note the two places *1* and *2* (VI) where the paper would lie flat against the side of the funnel. Fold each of these sections in half, forming two smaller flutings, only half as deep as the others. Strengthen all of the flutings by creasing lightly a second time, and the paper is ready for use.

Experiment 2

PURIFICATION BY CRYSTALLIZATION

(A) **Crystallization from Water.** Weigh out 10 g. of impure acetanilide from the bottle labelled "Impure Acetanilide for Recrystallization" [1] and transfer it to a 400–600-cc. beaker or Erlenmeyer flask. Add about 100 cc. of hot water and bring the mixture to the boiling-point (note that the acetanilide melts to a heavy oil in the hot solution). Add successive *small portions* of hot water, while stirring the mixture and boiling gently, until the acetanilide has dissolved completely. The objective is to dissolve the acetanilide in *slightly more* than the minimum amount of hot solvent. Do not attempt to dissolve resins, mechanical impurities, etc.

To the hot solution add 1–2 g. of decolorizing charcoal (Norite, Darco, boneblack, etc.) and boil for a short while longer, to aid in removing small amounts of colored impurities. Meanwhile prepare a funnel, a fluted filter (see page 27), and a clean beaker to receive the filtrate. The funnel should be at least 120 mm. in diameter and should have a very short stem (15–30-mm.).

Heat the funnel by inverting on a steam-bath, dry with a clean towel, and without allowing the funnel or the solution to cool, place the fluted filter in the funnel and pour the solution into the filter. Collect the hot filtrate in a beaker. If the solution cannot be poured into the filter in a single portion, replace it on the wire-gauze and continue to heat with a small flame to prevent cooling. As soon as all of the solution has been filtered, cover the beaker containing the hot filtrate with a watch glass and cool rapidly, with stirring, to room temperature or below. Allow to stand with occasional stirring until the product has separated completely. Filter the crystals with suction on a Büchner funnel and wash the crystals twice with a little cold water (see page 26), then press them on the funnel with a clean spatula or cork. Spread the crystals on a large clean paper, allow to dry completely, and weigh. Determine the

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[1] A method of preparing satisfactory material for this purpose is given in the appendix (page 396).

melting-point and if the product is not sufficiently pure (as shown by melting completely within a 1–2° temperature range), crystallize again in a similar manner.

(B) **Crystallization from an Inflammable Solvent.** Inflammable solvents such as ether, alcohols, benzene, etc., must never be heated in an open flask or beaker over a burner, nor manipulated near a flame. These solvents are usually heated on a steam-bath, or electric hot plate (having no exposed hot filament), preferably in an Erlenmeyer flask rather than a beaker.

Weigh out 10 g. of "Impure Naphthalene for Recrystallization" [1] and transfer it to a 125–150-cc. Erlenmeyer flask. Add 40 cc. of 95 per cent ethyl alcohol and warm the mixture *on a steam-bath* until the solvent boils. Add successive small portions of alcohol (not more than 10–12 cc. total) and boil gently after each addition, until the naphthalene has dissolved. Do not attempt to dissolve admixed particles of sand, grit, etc. Meanwhile prepare a fluted filter (see page 27) and arrange a funnel (65-mm. diam., 10–20-mm. stem) and clean dry flask to receive the filtrate.

Remove the boiling solution from the steam-bath, add 0.5 g. of decolorizing charcoal (*caution*—frothing), and shake well. Re-heat to boiling and pour the hot solution into the fluted filter.[2] Allow the filtrate to cool to room temperature, with occasional shaking. Filter the crystals with suction in a Büchner funnel (see page 26); wash all of the crystals into the funnel by rinsing the Erlenmeyer flask with part of the filtrate. Discontinue the suction and wash the crystals with 5–10 cc. of fresh alcohol (cold). Apply suction again and press the crystals firmly with a cork or flat glass stopper. Spread the crystals on a large clean paper and allow to dry thoroughly. Record the weight of purified naphthalene and determine its melting-point.

QUESTIONS

1. What general properties are necessary in a solvent in order that it be suited for the recrystallization of a particular organic compound?
2. By the procedure described above, what kinds of impurities may be removed from the acetanilide (or naphthalene)?

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[1] A method of preparing satisfactory material for this purpose is given in the appendix (page 396).

[2] Occasionally a few fine particles of the decolorizing agent may pass through the pores of the filter paper. Often this may be remedied by heating the filtrate to boiling and filtering again through the same filter.

DISTILLATION

Molecules of liquids (and of solid substances), even at temperatures far below their boiling-points, tend to escape from the surface and become gaseous molecules in the surrounding space. This escaping tendency of the molecules of a pure compound is a characteristic and constant property at a fixed temperature, and is called the vapor pressure or vapor tension. The vapor pressure is commonly expressed in terms of the height of a mercury column, in millimeters, which will produce an equivalent pressure. The vapor pressure of a pure compound is altered by the presence of dissolved substances, and by changing the temperature. Vapor pressure always increases with rise in temperature, and at the boiling-point the vapor pressure equals the atmospheric pressure.

Distillation consists in the vaporization of a liquid and subsequent condensation of the vapors. The objective of distillation is to separate a volatile liquid from a non-volatile substance, or to separate two or more liquids of different boiling-points. The boiling-point of a liquid is defined as the temperature at which the vapor pressure is equal to the total pressure upon the liquid. For ordinary distillation the pressure upon a liquid is the atmospheric pressure. For very accurate work it is necessary to record the barometric pressure during distillation, but for ordinary work the variation in boiling-point due to variations in atmospheric pressure may be neglected.

Since the boiling-point varies with the pressure upon the liquid, it is possible to lower the boiling-point appreciably by effecting distillation in a closed system under reduced pressure (1–30 mm.). In this way, substances which decompose upon heating to the boiling-point under atmospheric pressure (760 mm.) may be distilled without decomposition at a lower temperature under reduced pressure; for example, glycerine, which boils with decomposition at 290° under 760 mm. pressure, boils without decomposition at 180° under 12 mm. pressure.

In order to effect separation of a mixture into its constituents by distillation, it is essential that the boiling-points of the individuals be different. The ease of separation depends upon the magnitude of these differences. If only one component of a mixture is volatile, there is no difficulty in obtaining it in a pure state by distillation, and in many cases a mixture of several volatile liquids may be separated.

The volatile impurities that accompany a liquid may be divided into two general types—those which are more volatile and those which are less volatile than the liquid. When a liquid containing both types of impurity is subjected to distillation, as the temperature rises the first portion of distillate (called the fore-run, or low-boiling fraction) will contain the more volatile impurity and a certain amount of the main liquid which it carries with it. As the temperature continues to rise, the bulk of the principal liquid will then distil over a short temperature range, usually 2–3° (called the principal fraction). After this fraction has distilled, the boiling-point will rise, due to the presence of the less volatile impurity. The next fraction (called the after-run, or high-boiling fraction) will consist of a mixture of the principal liquid and the less volatile impurity. The residual liquid in the distilling flask will contain the less volatile impurity along with some of the principal liquid which it may hold back from distilling. Whether a pure liquid or an impure liquid is distilled, a small portion is always left in the flask at the end of the procedure. This results from condensation of the vapor required to fill the distilling flask. In order to minimize this quantity, it is advisable to use a distilling flask of the proper size and not one which is too large. A distilling flask is of the proper size when it is filled to one-half its capacity at the beginning of the distillation.

CALIBRATION OF THERMOMETERS

Two important errors affect the temperature readings which are registered directly on an ordinary thermometer in the course of laboratory distillations: (1) errors caused by exposure of a portion of the mercury column to atmospheric cooling, (2) errors due to inaccurate and incorrect graduation of the thermometer scale.

When a typical long-scale thermometer is used, the true boiling-point is not observed because the mercury column is not entirely at the temperature of the mercury in the bulb of the thermometer.

The portion of the mercury column which extends above the cork is cooled by the surrounding atmosphere, and the registered temperature is therefore below the true temperature of the vapor in the distilling flask. In the case of temperatures below 100° this cooling effect does not cause any considerable error, but for high temperatures the observed reading may be from 3–6° below the true temperature. This error can be corrected by adding a "stem correction," calculated by the formula:

Stem Correction (in degrees) = $0.000154(t - t')N$.

0.000154 = coefficient of apparent expansion of mercury in glass.

N = number of degrees on the stem of the thermometer from the lower exposed level to the temperature read.

t = temperature read; t' = average temperature of the exposed mercury column.

In practice, this correction is subject to an error since t' is not accurately known. Nevertheless, this correction is frequently used in ordinary work.

Many important errors of temperature readings in ordinary laboratory work may be due to incorrect graduation and calibration of the thermometer scale. To determine whether or not a thermometer registers correctly it may be tested by verification at several temperatures against the boiling-points of pure liquids or the melting-points of pure solids, or by comparison with previously standardized short-scale thermometers (Anschütz thermometers, each of which has a range of only 60–70°).

Table III

REFERENCE TEMPERATURES FOR CALIBRATION

Boiling Points, Deg. C., at 760 mm. Pressure *		Melting Points, Deg. C.	
Acetone	56.1	Water-Ice	0.0
Water	100.0	1,3-Dinitrobenzene	89.7
Ethylene Bromide	131.6	Benzoic Acid	121.7
Aniline	184.4	Benzilic Acid	150
Nitrobenzene	210.9	Hippuric Acid	187.5
α-Bromonaphthalene	281.1	3,5-Dinitrobenzoic Acid	204
Benzophenone	305.9	Cinchonine	264

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* If the atmospheric pressure during standardization is other than 760 mm., the boiling-point may be calculated by the Rule of Crafts: see Washburn, *Principles of Physical Chemistry*, pages 68–70, McGraw-Hill Book Co., New York (1921).

The most satisfactory way to determine the true temperatures which correspond to observed temperature readings is to calibrate the thermometer against a standardized short-scale thermometer, using the same conditions under which the thermometer is to be employed. Thus, a thermometer may be calibrated for a fixed partial immersion of the stem; for example, a thermometer to be used for distillation may be calibrated for 3-inch (76-mm.) immersion of the stem, one to be used for melting-point determinations may be calibrated for 1-inch (25-mm.) immersion of the stem.

Experiment 3

DETERMINATION OF BOILING-POINTS

Arrange a distillation apparatus in the following way: Attach the side-tube of a 50–60-cc. distilling flask by means of a properly bored cork to a water-cooled condenser set downward for distillation (see Fig. 7). Provide the mouth of the flask with a cork holding a thermometer, placed so that the top of the mercury bulb is 5–10 mm. below the opening of the side-tube. Place two small chips of clay plate in the flask to prevent bumping and superheating, and arrange an ordinary flask or a distilling flask at the end of the condenser to serve as a receiver.

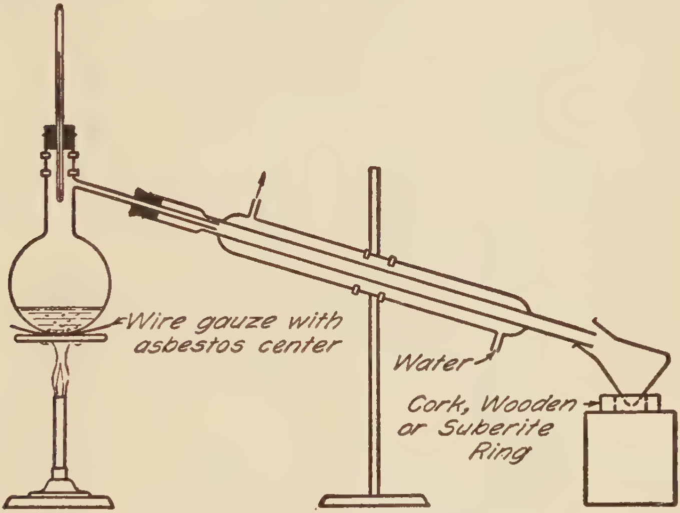
Wire gauze with asbestos center
Water
Cork, Wooden or Suberite Ring

Fig. 7.—Apparatus for Distillation.

Calibration of Thermometers. Before proceeding with the determination of boiling-points, the thermometer should be tested at 0°, by immersion in a bath of ice and distilled water, and at 100°, by distilling pure water in the apparatus. The apparatus should then be disconnected and dried thoroughly, as described below, before attempting to distil the benzene.

Drying of Apparatus. Distilling flasks and other glassware may be dried rapidly and conveniently by rinsing with a little acetone (5–15 cc.), and then drawing or passing a current of *dry air* through the apparatus. Ordinary compressed air is not suitable for drying purposes unless a good drying train is used, since it is apt to be nearly saturated with water and may even contain suspended droplets of water. Often it is more convenient to draw a stream of air through the apparatus by means of a glass tube connected to a suction pump.

It is also suitable to dry apparatus by washing with a little alcohol, followed by ether, and passing a current of dry air through the apparatus. A small piece of *thin-walled* glassware can be dried merely by warming over a flame, while keeping the piece in constant motion and drawing air through it.

Distillation. (A) In a dry distilling flask place 25 cc. of pure benzene, adjust all of the corks in place, and make certain that all connections are tight. Heat the flask on an asbestos-centered wire-gauze with a small flame and observe the temperature when the first drops of benzene are condensed in the condenser. Continue to distil until all but 5–10 cc. of the benzene has passed over, and note the temperature at regular intervals during the distillation. Record the temperature range from the beginning to the end of the distillation; this is the observed boiling-point. Return the used benzene to a bottle provided for this purpose on the side-shelf.

(B) In the same apparatus, place 25 cc. of a mixture of benzene and toluene (or carbon tetrachloride and toluene) and distil, following the same procedure used for pure benzene.

QUESTIONS

1. Define accurately the term boiling-point.
2. What is the effect upon the boiling-point of reducing the external pressure?
3. From your results what general conclusions may be drawn as to the behavior of pure liquids and of mixtures when subjected to distillation?

FRACTIONAL DISTILLATION[1]

The separation of mixtures by means of fractional distillation and fractionating columns depends upon these general principles: when a typical liquid mixture is *partially* vaporized the resulting vapor is richer in the more volatile component than was the original mixture, and when a vapor mixture is *partially* condensed the condensate contains less of the more volatile component than did the vapor.[2] It is evident, therefore, that a series of distillations involving partial vaporization and condensation will concentrate the

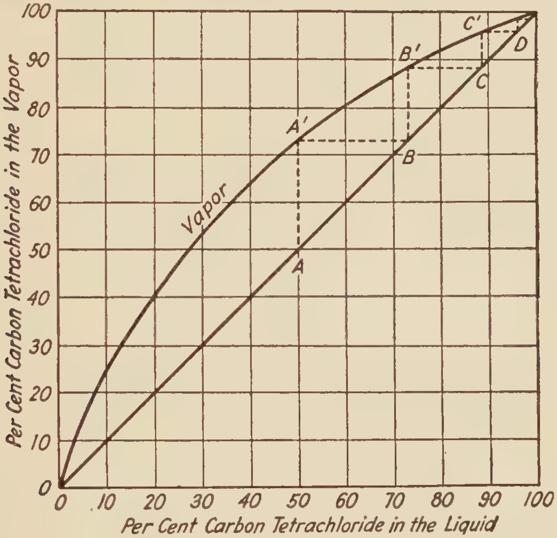

FIG. 8.—Liquid-Vapor Composition Curve for Mixtures of Carbon Tetrachloride and Toluene.

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[1] Excellent reference books on this subject are: Sidney Young, *Distillation Principles and Processes*, Macmillan and Co., London (1922); Morton, *Laboratory Technique in Organic Chemistry*, pages 73–97, McGraw-Hill Book Co., Inc., New York (1938); Robinson and Gilliland, *The Elements of Fractional Distillation*, McGraw-Hill Book Co., Inc., New York (1939).

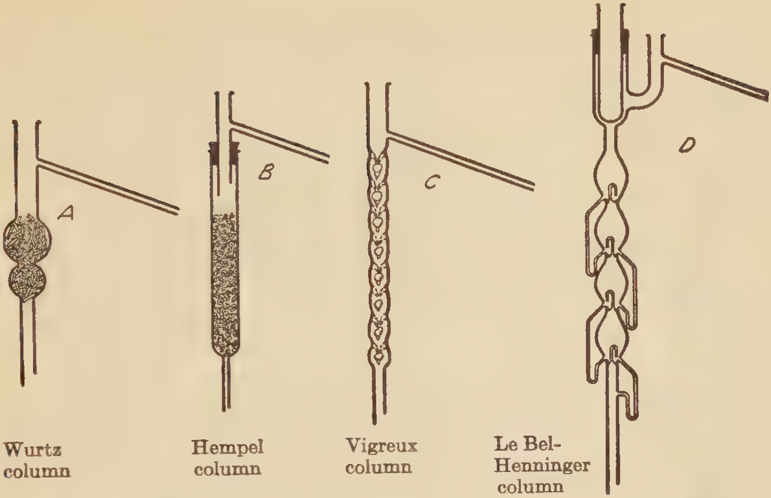
[2] There are some notable exceptions to these broad generalizations; they do not hold true for all mixtures of partially miscible liquids, for immiscible liquids (see Steam Distillation, page 53) or for constant-boiling mixtures (see Azeotropic Mixtures, page 45).

more volatile component in the first fraction of distillate and leave the less volatile component in the last fraction, or in the residual liquid.

In Fig. 8 are shown the relations of liquid and vapor composition for mixtures of carbon tetrachloride (b.p. 77°) and toluene (b.p. 111°), as determined by actual experiments. The percentage by weight of carbon tetrachloride in the liquid mixtures is plotted on the x-axis, and the percentage of carbon tetrachloride in the vapor in equilibrium with a given liquid mixture is plotted on the y-axis; the percentage of toluene in the mixtures is obtained by subtracting the carbon tetrachloride content from 100 per cent. The 45° diagonal (liquid line) can be used to show the effect of a series of small scale *separate* distillations in concentrating the more volatile component. A liquid mixture containing 50 per cent carbon tetrachloride (point A, on the liquid line) is in equilibrium with vapor containing 73 per cent carbon tetrachloride (point A', on the vapor curve). If the liquid A is *partially* vaporized and the vapor A' condensed completely (as in any simple distillation) the condensate will be represented by B (on the liquid line). Repetition of this process yields a new distillate C, containing 88 per cent carbon tetrachloride, and eventually a small amount of practically pure material could be obtained. This procedure would be exceedingly tedious, and wasteful of time and materials.

A fractionating column is designed to provide a continuous series of partial condensations of the vapor and partial vaporizations of the condensate, and is similar in effect to a number of separate distillations. A column consists essentially of a long vertical tube, or series of bulbs, through which the distilling vapor passes upward and is partially condensed; the condensate flows down the column and is returned eventually to the distilling flask. In the column the returning liquid is brought into intimate contact with the ascending vapor and a heat interchange occurs, whereby the vapor is enriched in the more volatile component at the expense of the liquid. To obtain a good separation it is necessary to have a large amount of liquid continually returning through the column, a thorough mixing of liquid and vapor, and a large active surface of contact between liquid and vapor.

The simple laboratory fractionating columns are not sufficiently effective to allow the complete separation, by a single distillation, of two liquids whose boiling points are close together. The mixture is separated by a first distillation into a number of fractions of progressively higher boiling point, and these are refractionated separately in a systematic way until a fairly complete separation of



Wurtz column

Hempel column

Vigreux column

Le Bel-Henninger column

Fig. 9.—Laboratory Fractionating Columns.

the components is achieved. With mixtures of closely related substances, such as benzene (b.p. 80°) and toluene (b.p. 111°), the separation is often difficult even when the difference in boiling-points is fairly large. Table IV illustrates a typical laboratory fractionation of a benzene-toluene mixture, using a simple column.

TABLE IV

FRACTIONAL DISTILLATION OF BENZENE–TOLUENE MIXTURE CONTAINING 100 G. OF EACH COMPONENT *

Fraction	Temperature Interval in Deg. C.	Weight of Fraction in Grams			
		1st Dist'n	2d Dist'n	3d Dist'n	4th Dist'n
1	80–85	—	37	59	70
2	85–91	60	42	26	17
3	91–99	40	26	16	10
4	99–105	34	18	12	8
5	105–111	53	50	48	43
Residue	Above 111	11	23	32	42
Total Weight of Distillate. . .		198 g.	196 g.	193 g.	190 g.
Total Losses during Manipulation.		2 g.	4 g.	7 g.	10 g.

* The values given in this chart are such as can be obtained under ordinary laboratory conditions using a small two-bulb column. The exact weights of various fractions, however, are so dependent upon rate of distillation, type and size of column, and on other physical conditions, that the chart is valuable merely as an indication of what may be expected.

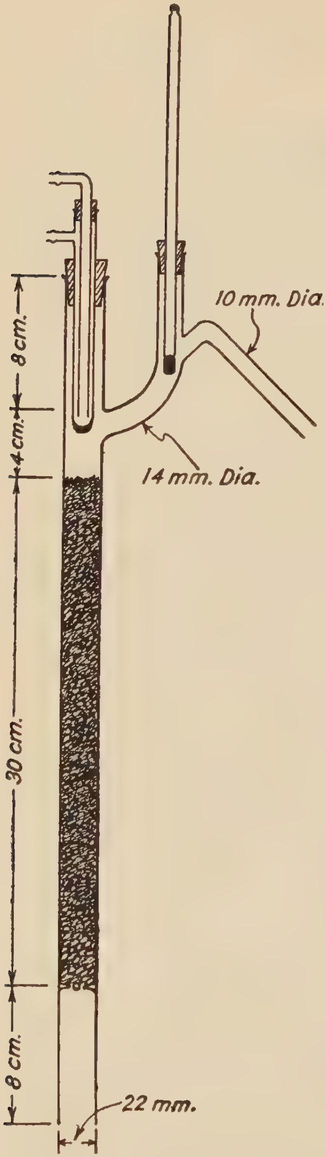


Fig. 10.—Packed Column with Dephlegmator.

In the simpler and less efficient columns (Fig. 9, *A*, *B*, *C*) returning liquid is provided merely by atmospheric cooling of the vapor in the upper portion of the column (but the main portion should be insulated to avoid excessive heat loss). In more elaborate columns an adequate quantity of refluxing liquid is obtained by placing a small partial condenser ("cold finger") at the top of the column. The partial condenser (dephlegmator) can be raised or lowered to decrease or increase the amount of refluxing liquid. The *reflux ratio* expresses the quotient of the amount of liquid returning through the column to the amount collected in the receiver during the same time interval.

Increasing the length of a column or the reflux ratio improves the efficiency of separation but care must be taken to avoid flooding the column with liquid. Flooding diminishes the contact area between vapor and liquid, and the pressure of ascending vapor may force the liquid upward in the column. To obtain good heat exchange between vapor and liquid, and to avoid flooding, a column should be well insulated. For liquids that distil below 100° a wrapping of asbestos paper is usually sufficient; for higher boiling liquids or very long columns, an evacuated or electrically heated jacket may be used.

Effective contact between liquid and vapor is obtained in the various types of fractionating columns either by dividing the column into sections and allowing the vapor to bubble through the condensate in each section (bubbling columns), or by allowing the returning liquid to spread in a thin film over a large surface of inert packing material (packed columns). In a packed column it is essential to leave sufficient free space for the countercurrent flow of liquid and vapor. Crushed carborundum (6-mesh), glass spirals, and hollow glass or metal cylinders (Raschig or Lessing rings) are effective packing materials for small laboratory columns. A small, relatively efficient and inexpensive, packed column of good design, with a "cold-finger" dephlegmator, is shown in detail in Fig. 10.

Azeotropic Mixtures (Constant-Boiling Mixtures)

Not infrequently, liquids which may differ widely in boiling-point form *azeotropic mixtures* of definite and constant composition which have a constant boiling-point and behave like a single pure liquid. The components of an azeotropic mixture cannot be separated by fractional distillation since the vapor in equilibrium with

Table V

BINARY AZEOTROPIC MIXTURES

Component A		Component B		Azeotropic Mixture		
Substance	Boiling-Point	Substance	Boiling-Point	Percentage of A (weight)	Percentage of B (weight)	Boiling-Point
Acetone.....	56.4°	Chloroform	61.2°	20	80	64.7° (maximum)
Nitric Acid..	86.0°	Water	100.0°	68	32	120.5° (maximum)
Formic Acid.	100.7°	Water	100.0°	77.5	22.5	107.3° (maximum)
n-Propyl Alcohol...	97.2°	Water	100.0°	71.7	28.3	87.7° (minimum)
tert.-Butyl Alcohol...	82.5°	Water	100.0°	88.2	11.8	79.9° (minimum)
Ethyl Alcohol	78.3°	Water	100.0°	95.6	4.4	78.15° (minimum)
Ethyl Alcohol	78.3°	Toluene	110.6°	68	32	76.7° (minimum)
Acetic Acid..	118.5°	Toluene	110.6°	28	72	105.4° (minimum)

the liquid has the same composition as the liquid itself (as is the case for a pure individual). These mixtures may have a boiling-point below that of either component (minimum boiling-point) or a boiling-point above that of either component (maximum boiling-point). The accompanying table gives the composition and boiling-point of a number of examples of azeotropic mixtures containing two components (binary systems). Azeotropic mixtures containing three components (ternary systems) are also encountered; for example, benzene-water-ethyl alcohol (see page 75), ethyl alcohol-water-ethyl acetate, etc.

Experiment 4

PURIFICATION BY FRACTIONAL DISTILLATION

Arrange in the following way an apparatus for fractional distillation. Provide a 200-cc. round-bottom flask with a Wurtz column having at least two bulbs, or other suitable column. Fit the column with a cork holding a thermometer, placed so that the top of the mercury bulb is 5–10 mm. below the opening of the side-tube, and connect the side-tube to a water-cooled condenser (60–70 cm. in length) set downward for distillation. The fractionating column may be rendered more effective by filling the bulbs with short pieces of glass tubing, from 15–30 mm. in length (see Fig. 11), and wrapping the column with asbestos paper. Prepare five clean, dry receivers (50–150-cc. Erlenmeyer flasks) and mark them A, B, C, D, and E (residue). Provide all of the receivers with clean tightly-fitting corks.

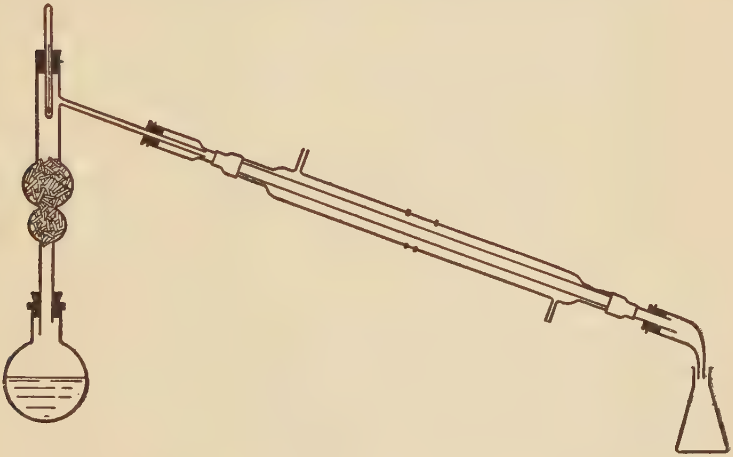


Fig. 11.—Apparatus for Fractional Distillation.

Have the set-up approved by the laboratory instructor and note the precautions (page 51) before starting the distillation.

Carbon Tetrachloride and Toluene. In the 200-cc. round-bottom flask place 120 cc. of a mixture of carbon tetrachloride and toluene which contains about equal volumes of each. Add a few small chips of clay plate, and heat the flask on an asbestos-centered wire-gauze over a small flame. As soon as the mixture starts to boil, regulate the flame especially carefully so that the liquid distils *slowly* and *regularly*. In the first distillation, collect the fraction which distils from 76–81° in flask A, from 81–88° in flask B, from 88–98° in flask C, from 98–108° in flask D. After fraction D has distilled, extinguish the flame, cool the flask, allow the column to drain, disconnect the flask, and pour the residue into E. Measure the volume of each fraction and record the results in tabular form.

Table VI

FRACTIONAL DISTILLATION OF CARBON TETRACHLORIDE AND TOLUENE MIXTURE

Fraction	Temperature Range	Volume of Fractions in cc.				
		1st Dist'n	2d Dist'n	3d Dist'n	4th Dist'n	5th Dist'n
A	76–81°					
B	81–88°					
C	88–98°					
D	98–108°					
E	residue					
Total Volume of Fractions						

In the subsequent distillations proceed in the following way: Pour the contents of flask A into the round-bottom flask and redistil, collecting the distillate from 76–81° in the same flask A. When the thermometer reaches 81°, stop the distillation and add the contents of flask B. Continue the distillation and collect the fraction from 76–81° in flask A, and from 81–88° in flask B. When the thermometer reaches 88°, stop the distillation and add the contents of flask C. Continue the distillation and collect the fraction from 76–81° in flask A, from 81–88° in flask B, and from 88–98° in flask C. When the thermometer reaches 98°, stop the distillation and add the contents of flask D. Continue the distillation and collect the fractions A, B, C, and D. When the thermom-

eter reaches 108°, stop the distillation and add the contents of flask E. Continue the distillation and collect the fractions A, B, C, and D. After fraction D has distilled, extinguish the flame, cool the flask, allow the column to drain, disconnect the flask, and pour the residue into E. Measure the volume of each fraction and record the results in tabular form.

If B, C, and D at this stage contain a total of more than 15–20 cc. of liquid, carry out a third distillation in the same manner. If necessary, carry out a fourth or fifth distillation, so that the fraction A will contain almost all of the carbon tetrachloride and the residue E almost all of the toluene. To remove mechanical impurities and coloring matter, and to obtain almost pure toluene, E may be redistilled from a small distilling flask without a column.

➔ **Caution:** Extinguish or remove the flame when transferring fresh fractions into the round-bottom flask, since toluene has a high vapor pressure and is inflammable. If the lower end of the condenser is fitted with an adapter, there is usually less loss of material by evaporation. A *loose* plug of cotton between the condenser tube and the receiver will also diminish the evaporation losses. Care must be taken to prevent the cotton from coming in contact with the distillate.

Benzene and Toluene. A mixture of benzene and toluene may be separated by the procedure outlined above, if the bulbs of the column are filled with short pieces of glass tubing to increase the efficiency of the fractionation. The following ranges are satisfactory for the fractions: A, from 80–85°; B, from 85–91°; C, from 91–99°; D, from 99–106°; E, residue.

Chloroform and Toluene. For the separation of a mixture of chloroform and toluene, the following temperature ranges are satisfactory for the fractions: A, from 62–68°; B, from 68–78°; C, from 78–95°; D, from 95–106°; E, residue.

Methyl Alcohol and Water. For the separation of a mixture of methyl alcohol and water, the following temperature ranges are satisfactory for the fractions: A, from 65–70°; B, from 70–80°; C, from 80–90°; D, from 90–95°; E, residue.

QUESTIONS

1. Why is it necessary to have liquid flowing back through the fractionating column in order to obtain efficient fractionation?

2. What is an azeotropic mixture, and why cannot its components be separated by fractional distillation? Explain fully.

STEAM DISTILLATION

Mixtures of two immiscible substances behave quite differently from homogeneous solutions and are subject to different physical laws. When liquids which are mutually insoluble (or practically so) are heated together, each component vaporizes independently of the other, and a mixture of the two components distils when the sum of the separate vapor pressures attains a value equal to the external pressure.

Since the temperature at which the mixture distils will be lower than the boiling-point of either component, it is possible to effect the "steam distillation" of a high-boiling liquid at a temperature much below its boiling-point without using distillation under diminished pressure. The process of steam distillation is frequently used for the isolation of organic substances such as bromobenzene, aniline, nitrobenzene, and many essential oils.

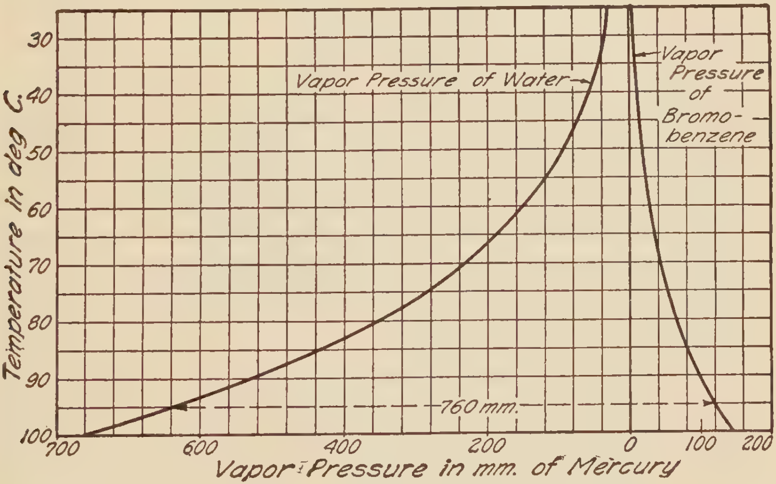


FIG. 12.—Vapor Pressure Curves.

If the vapor pressure curves of the components are known, the distillation temperature of the mixture can easily be determined. This is most readily done by plotting the vapor pressure curves in such a way that the sum of the vapor pressures at any temperature may easily be measured. If the distillation temperature of the mixture and the vapor pressures of the pure components at this temperature are known, the composition of the distillate can be calculated by Dalton's law of partial pressures.

The application of the general principles mentioned above may be made clearer by considering a specific case, such as the steam distillation of bromobenzene and water. Since the sum of the individual vapor pressures (see page 53) attains 760 mm. at 95°, the mixture will distil at this temperature. At 95° the vapor pressures are: bromobenzene—120 mm., water—640 mm. According to Dalton's law the vapor at 95° will be composed of molecules of bromobenzene and of water in the proportion of 120 to 640. The proportion by weight of the components can be obtained by introducing their molecular weights:

$$\frac{\text{Weight of Bromobenzene}}{\text{Weight of Water}} = \frac{120 \times 157}{640 \times 18} = \frac{157}{96}$$

The weight composition of the distillate will therefore be 62 per cent bromobenzene and 38 per cent water:

$$\text{Bromobenzene} = \frac{157}{96 + 157} \times 100 = 62 \text{ per cent}$$

$$\text{Water} = \frac{96}{96 + 157} \times 100 = 38 \text{ per cent}$$

From the above considerations, it can be seen that there are several requirements for the actual use of steam distillation in the laboratory: the substance to be steam distilled must be practically immiscible with water, must not be decomposed by prolonged boiling with water, and must have an appreciable vapor pressure (5–10 mm. at least) in the vicinity of 100°. To meet certain special conditions, laboratory methods have been devised for using steam distillation under diminished pressures, and for using superheated steam.

Experiment 5

STEAM DISTILLATION

Arrange in the following way an apparatus for steam distillation. Conduct steam from the laboratory supply line [1] through a rubber tube to a 1-l. Florence flask, which serves as a trap [2] to remove foreign matter from the pipe line and to remove mechanically-carried water. Fit the Florence flask with a three-hole stopper which holds a steam inlet tube extending 50–75 mm. through the stopper, a steam outlet tube extending only 5–10 mm. through the stopper, and a water outlet tube reaching to within 10 mm. of the bottom of the flask (see Fig. 13). Provide the water outlet tube with a long rubber tube conducting to a drain and fitted with a screw clamp to regulate the flow. During the experiment adjust the screw clamp so that the rate at which the water drains is about equal to the rate at which it collects in the trap.

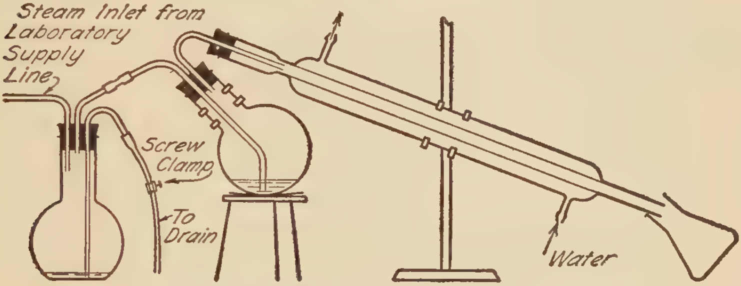


FIG. 13.—Apparatus for Steam Distillation.

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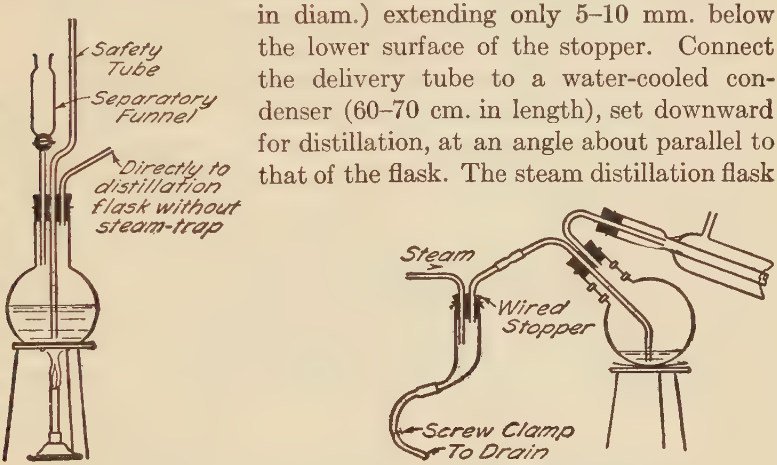
[1] If steam is not available in the laboratory, it may be generated conveniently by boiling water in a 1-l. Florence flask (see Fig. 14). In this case, provide the generating flask with a three-hole stopper which holds a steam outlet tube, a safety tube (50–60 cm. in length) extending nearly to the bottom of the flask, and a cylindrical separatory funnel (to introduce more water if necessary). Support the generating flask on an asbestos-centered wire-gauze, introduce 500–600 cc. of water, and add a few small chips of clay plate to produce regular ebullition. Heat the water rapidly to boiling and adjust the flame so as to obtain a steady current of steam. Pass the steam directly into the distillation flask without using a trap.

[2] In place of the Florence flask, an adapter may be arranged to serve as a suitable trap (see Fig. 14).

Conduct the steam from the trap, or from the generating flask, into a 1-l. round-bottom flask (preferably with long neck) which is supported on an asbestos-centered wire-gauze and tipped at an angle of 30–45° from the vertical. Fit the flask with a two-hole stopper holding a steam inlet tube which dips below the surface of the mixture to be distilled, and a wide delivery tube (about 8 mm. in diam.) extending only 5–10 mm. below the lower surface of the stopper. Connect the delivery tube to a water-cooled condenser (60–70 cm. in length), set downward for distillation, at an angle about parallel to that of the flask. The steam distillation flask may be heated gently, with a small flame, to avoid the condensation of too large an amount of water due to atmospheric cooling.



Steam generator

Adapter steam trap

FIG. 14.—Steam Distillation Accessories.

Have the set-up approved by the laboratory instructor before starting the distillation. Make sure all connections are tight.

(A) In the round-bottom flask, place 30 g. (20 cc.) of bromobenzene[1] (b.p. 155° at 760 mm.) and about 50 cc. of water, and pass a rapid, steady current of steam into the mixture. Continue to distil with steam until a test portion of the distillate shows that no more water-insoluble material is passing over. When the distillation is finished, open the screw clamp of the drain tube and disconnect the distillation flask *before* shutting off the steam (Why?).

Transfer the distillate, which is a mixture of bromobenzene and water, to a separatory funnel and separate the layer of bromobenzene. Pour this into the bottle on the side-shelf labelled "Used Bromobenzene."

---

[1] Consult the appendix, "Vapor Pressures of Organic Substances and of Water."

(B) Determine the melting-point of the samples of *p*-dichlorobenzene and of salicylic acid which are to be used in this experiment.

In a clean porcelain mortar, mix thoroughly 5 g. of *p*-dichlorobenzene [1] and 5 g. of salicylic acid,[2] and determine the melting-point of the mixture. Transfer the mixture to the steam distillation flask, add about 50 cc. of water and distil with a rapid, steady current of steam exactly as described in the above experiment. When no more water-insoluble material passes over, open the screw clamp, disconnect the distillation flask and shut off the steam. Save the distillate and the residue in the round-bottom flask for further examination.

➔**Caution:** Since the material which distils with steam may solidify in the condenser, watch carefully to avoid the formation of a crystalline mass which will completely obstruct the condenser tube. If a large crystalline mass collects in the tube, stop the flow of water through the condenser *momentarily* and drain the water from the condenser jacket. The heat from the vapors will then melt the crystals and the obstruction will be removed. As soon as this occurs, start the water again through the condenser jacket.

Before the residue in the flask has had an opportunity to cool, filter the solution through a fluted filter, and collect the filtrate in a clean beaker. Cool the solution rapidly to room temperature or below, and filter the crystals with suction in a Büchner funnel. Allow the crystals to dry and determine their melting-point. What is this substance which did not distil with steam?

Separate the solid material in the distillate by filtering with suction, and press it as dry as possible with a clean cork or spatula. Allow the crystals to dry completely and determine their melting-point. What is the substance which distilled with steam?

QUESTIONS

1. Why is the steam distillation flask tipped at an angle?
2. What properties must a substance have in order that it may be practical to distil it with steam?
3. What are the advantages and disadvantages of steam distillation as a method of purification?

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[1] Consult the appendix, "Vapor Pressures of Organic Substances and of Water."

[2] Consult the appendix, "Vapor Pressures of Organic Substances at 100° C."

EXTRACTION WITH SOLVENTS

The process of extraction with solvents is used in organic chemistry for the separation and isolation of substances from mixtures which occur in nature, for the isolation of dissolved substances from solutions, and for the removal of soluble impurities from mixtures.

The extraction of alkaloids from leaves and bark, flavoring extracts from seeds, perfume essences from flowers, and sugar from sugar cane, are examples of extractions of the first type. Solvents which are commonly used for this purpose are: ether, chloroform, carbon disulfide, acetone, various alcohols, and water.

A very common form of apparatus for continuous extraction of solids by means of volatile solvents is called a Soxhlet Extractor. A typical laboratory set-up employing this extraction device is shown mounted and ready for use, in Fig. 15.

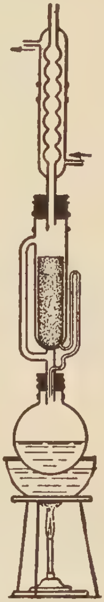

FIG. 15.—Soxhlet Extractor with Accessories.

The isolation of dissolved organic substances from solution is often accomplished by extraction with an immiscible solvent. The general principle underlying this process is known as the distribution law. In dilute solutions a substance distributes itself between two immiscible solvents so that the ratio of the concentration in one solvent to the concentration in the second solvent always remains constant (at constant temperature). This constant ratio of concentrations for the distribution of a solute between two particular solvents is called the distribution-coefficient or the partition-coefficient for the substance between the two solvents.

Distribution Coefficient[1] of X between solvents A and B

$$= \frac{\text{Concentration of } X \text{ in } A}{\text{Concentration of } X \text{ in } B} = K \text{ (at constant temperature).}$$

---

[1] In the case of dissolved substances which are ionized or associated in one of the solvents, the distribution law holds true for the ratio of the concentrations of

In practice the most common application of this law is the extraction of dissolved substances from aqueous solutions by almost immiscible[1] solvents such as ether, benzene, and chloroform.

The theoretical considerations involved in these extractions may be illustrated by a specific example, such as the extraction of butyric acid from an aqueous solution by the solvent benzene.

Let us assume that the distribution-coefficient of butyric acid between water and benzene is $\frac{1}{3}$ at 20°. If we take an aqueous solution containing 6 g. of butyric acid in 100 cc. of water and extract at 20° with 100 cc. of benzene, the following equations may be written:[2]

$$(1)\quad \frac{C_w}{C_b} = \frac{\dfrac{W_w}{100}}{\dfrac{W_b}{100}} = \frac{1}{3} \qquad\qquad (2)\quad W_w + W_b = 6\text{ g.}$$

W_w = weight of butyric acid in water layer
W_b = weight of butyric acid in benzene layer
C_w = concentration of butyric acid in water layer
C_b = concentration of butyric acid in benzene layer

Since $W_w = 6 - W_b$ (from equation 2), we may write

$$\frac{\dfrac{6 - W_b}{100}}{\dfrac{W_b}{100}} = \frac{1}{3}; \qquad \text{whence} \qquad \begin{aligned} W_b &= 4.5\text{ g.} \\ W_w &= 1.5\text{ g.} \end{aligned}$$

After one extraction with 100 cc. of benzene, 4.5 g. of butyric acid (75 per cent of the total) is removed by the benzene, and 1.5 g. (25 per cent of the total) remains in the water.

The following question may arise in laboratory work if a limited quantity of solvent is available for use in extraction: Is it preferable to make a single extraction with the total quantity of the solvent, or to make a number of extractions with portions of the solvent?

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the simple molecules only. To obtain an expression which will hold for the total concentrations it is necessary to introduce an expression for the ionization or association equilibrium.

[1] Actually no two solvents are absolutely immiscible, but each solvent is at least slightly soluble in the other. Ether, a very common solvent for extraction, is somewhat more soluble than many solvents; for example, at 30° ether is soluble to the extent of 1 g. in 18.8 g. of water, and water is soluble to the extent of 1 g. in 73 g. of ether.

[2] The distribution-coefficients found in the chemical literature are usually expressed in concentrations per volume of solution. In making calculations it is much simpler to use concentrations per volume of solvent. For dilute solutions the error introduced in this way is negligible.

As far as efficiency of extraction is concerned, the second method is preferable. The theoretical basis for this conclusion is shown by a consideration of the example mentioned above.

In the extraction of the above aqueous solution of butyric acid with benzene, suppose that we extract twice with 50-cc. portions of benzene instead of making a single extraction with 100 cc. of the solvent. For the first extraction with 50 cc. of benzene, we can write the equation:

$$\frac{\frac{W_w}{100}}{\frac{W_b}{50}} = \frac{\frac{6 - W_b}{100}}{\frac{W_b}{50}} = \frac{1}{3}; \qquad \text{whence} \qquad \begin{array}{l} W_b = 3.6 \text{ g.} \\ W_w = 2.4 \text{ g.} \end{array}$$

The aqueous solution, which contains 2.4 g. of butyric acid, is then extracted with the second 50-cc. portion of benzene:

$$\frac{\frac{W_w}{100}}{\frac{W_b}{50}} = \frac{\frac{2.4 - W_b}{100}}{\frac{W_b}{50}} = \frac{1}{3}; \qquad \text{whence} \qquad \begin{array}{l} W_b = 1.44 \text{ g.} \\ W_w = 0.96 \text{ g.} \end{array}$$

The two combined benzene extracts have removed 5.04 g. of butyric acid (84 per cent of the total amount) and 0.96 g. (16 per cent of the total amount) remains in the water.

Since only 4.5 g. (75 per cent of the total amount) was removed by a single extraction with 100 cc. of benzene, it is obvious that the second method of extraction is considerably more efficient. As is to be expected from the above conclusions, three extractions with $\frac{1}{3}$ of the total quantity of solvent would be even more efficient. Thus, three extractions of the above aqueous solution with $33\frac{1}{3}$-cc. portions of benzene would remove 5.25 g. of butyric acid (87.5 per cent of the total amount), and leave only 0.75 g. (12.5 per cent of the total amount) in the water.

Problem. Calculate the amount of butyric acid which would be extracted by using four 25-cc. portions of benzene. Would this additional amount be sufficient to compensate for the labor of an additional extraction operation?

The removal of soluble impurities by extraction with an immiscible solvent is of great importance in the purification of organic substances. If a substance containing a soluble impurity is treated with an immiscible solvent, the impurity distributes itself (according to the distribution law) between the substance being purified and the immiscible solvent. Consequently a portion of the impurity will be removed by the immiscible solvent. If the distribution-coefficient is known, calculations similar to those made above (for the extraction of a dissolved substance from solution) may be made for the extraction of the impurity. It is also true in this type of extraction that several extractions with portions of the solvent are more efficient for the removal of an impurity than a single extraction with the total amount of solvent.

Extraction by Chemically Active Solvents. Extraction of an organic substance by means of a chemically inert, immiscible solvent depends merely upon simple solubility relations. Another type of extraction, of great importance, depends upon the use of a reagent that reacts chemically with the substance to be extracted. This method is used frequently to separate the components of a mixture, and also to remove small amounts of impurities in an organic compound. The principle of the method is to select a reagent that acts selectively upon the organic substances that are present. Obviously this method requires a good knowledge of the chemical behavior of organic compounds toward various reagents, as well as a knowledge of solubility relationships.[1]

Commonly used "reaction solvents" are: dilute aqueous alkalies (5 per cent sodium hydroxide or potassium hydroxide solutions); dilute aqueous mineral acids (5 per cent hydrochloric acid, etc.); cold concentrated sulfuric acid.

Dilute sodium hydroxide solution (also sodium carbonate or bicarbonate) can be used to extract an organic acid from its solution in an organic solvent, or to remove traces of acid that are present as an impurity in an organic preparation. The use of aqueous alkali depends upon the conversion of the free acid to the corresponding sodium salt, which is soluble in water or dilute alkali. Thus, *n*-butyric acid may be extracted quantitatively from a benzene solution by dilute sodium hydroxide because this reagent converts the acid to sodium *n*-butyrate, which is very soluble in water or dilute alkali but insoluble in benzene. Likewise, an organic acid or mineral acid present as impurity in a water-insoluble liquid or solid, can be removed by washing with dilute alkali.

Dilute hydrochloric acid can be used in a similar way to extract basic substances from mixtures, or to remove basic impurities. The use of dilute acids depends upon converting the base (amines, ammonia, etc.) into a water-soluble salt (amine hydrochloride, ammonium chloride, etc.). Thus, an acid amide such as acetanilide can be freed of traces of aniline by washing with dilute hydrochloric acid; the amide does not react with cold dilute acid, but the amine (aniline) is converted into the water-soluble salt, aniline hydrochloride (phenylammonium chloride).

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[1] For discussion of this method consult: Kamm, *Qualitative Organic Analysis*, John Wiley and Sons, Inc., New York (1932); Shriner and Fuson, *The Systematic Identification of Organic Compounds*, John Wiley and Sons, Inc., New York (1940).

Cold concentrated sulfuric acid can be used to remove unsaturated hydrocarbons, alcohols, ethers, esters, etc., present as impurities in inert compounds such as saturated hydrocarbons and alkyl halides. Olefins and alcohols are dissolved by chemical reaction to form alkyl hydrogen sulfates; ethers, esters, etc., form addition complexes that are soluble in concentrated sulfuric acid. Owing to its great reactivity this reagent has limited utility.

Solubility Relationships. The solubility of an organic compound in inert solvents (water, alcohol, ether, hydrocarbons, etc.) and in chemically active solvents is directly related to its molecular structure. Consequently one can predict solubility relations in a qualitative way for various classes of compounds by taking into account the structure of the solute and the physical and chemical characteristics of the solvent medium.

Solubility in a chemically active solvent depends upon chemical reaction to form a water-soluble salt, and is readily predicted from definite chemical knowledge of the solute and the solvent.

Solubility in an inert solvent may be predicted with fair success on the basis of empirical solubility rules:

(1) A substance is most soluble in that solvent to which it is most closely related structurally. Thus, simple alcohols are soluble in water, esters are soluble in alcohol and ether, etc.

(2) A compound having branched chains is more soluble in a given solvent than the straight chain isomer. Thus, *iso*- and *tert*-butyl alcohols are much more soluble than *n*-butyl alcohol in water.

(3) In any homologous series the higher members become more and more like hydrocarbons in their physical properties. Thus, in most homologous series containing only one functional group, the solubility in water falls below 4–5 per cent when the member attains five carbon atoms.

(4) Compounds of high molecular weight (polymers, etc.) are usually sparingly soluble in inert solvents. However, polymers often form colloidal dispersions in certain solvents.

(5) Liquids and low-melting solids are generally more soluble than high-melting solids in inert solvents.

These simple rules are a convenient guide to solubility relations but one must expect to encounter many exceptions in actual practice.

Solubility tests are often used as a preliminary step in the identification of organic compounds. The systematic outline developed by Kamm (page 66) affords an excellent survey of solubility relations.

SOLUBILITY TABLE (KAMM)[1]

Soluble in Water		Insoluble in Water				
				Indifferent Compounds of C, H, and C, H, O		
Soluble in Ether	Insoluble in Ether	Soluble in Dilute HCl	Soluble in Dilute KOH	Soluble in Cold Conc. H_2SO_4	Insoluble in Cold H_2SO_4	Indifferent Compounds Containing N or S *
I	II	III	IV	V	VI	VII
Alcohols (low mol. wt.)	Polybasic acids, hydroxy acids, etc.	Primary amines	Acids	Alcohols	Saturated aliphatic hydrocarbons	Nitro compounds (tertiary)
Aldehydes (low mol. wt.)	Polyhydroxy alcohols, sugars, and certain derivatives	Secondary amines	Phenols	Aldehydes	Aromatic hydrocarbons	Amides and negatively substituted amines
Ketones (low mol. wt.)	Some amides, amino acids, amines, etc.	Tertiary amines	Some amides, imides, etc.	Ketones and quinones	Saturated alkyl halides	Nitriles
Other neutral oxygenated compounds	Many sulfonic acids and other sulfur compounds	Hydrazines	A few nitro compounds and oximes	Ethers and acetals	Aryl halides	Azo and hydrazo compounds, etc.
Acids (low mol. wt.)	Many salts		Some thiophenols, sulfonic and sulfinic acids	Esters and lactones		Sulfones, sulfonyl derivatives of secondary amines
A few anhydrides			A few enols	Anhydrides		Mercaptans, sulfides, sulfates, etc.
A few esters, phenols, etc.				Unsaturated hydrocarbons		
Amines (low mol. wt.) Neutral nitrogen compounds						

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* Halogen compounds are not listed separately but are met in each of the seven groups in accordance with their solubility behaviors. Similarly certain nitrogen and sulfur compounds will fall in Groups I, II, III, and IV.

[1] Reprinted by permission from *Qualitative Organic Analysis* by Kamm, published by John Wiley & Sons, Inc.

Experiment 6

EXTRACTION WITH SOLVENTS

In a small Erlenmeyer flask, place 95 cc. of distilled water and add 5 cc. of glacial acetic acid. Mix thoroughly, measure the volume in a graduated cylinder, and divide the solution into two equal portions.

(A) Place one portion of the solution in a clean 250–300-cc. separatory funnel and extract with 150 cc. of ether in the following way. Stopper the separatory funnel, shake gently, and turn it upside down. While the separatory funnel is in this position, open the stopcock to release the internal pressure. Close the stopcock, shake vigorously, and again release the internal pressure. Repeat this procedure four or five times, then support the separatory funnel in a ring, and allow it to remain undisturbed. When the liquids have completely separated, draw off the lower aqueous layer into a clean Erlenmeyer flask and titrate with standard sodium hydroxide solution (about 1–N), using phenolphthalein as indicator. Calculate (a) the amount of acetic acid left in the water layer, (b) the amount extracted by the ether, (c) the percentage of the acetic acid left in the water, (d) the percentage extracted by the ether. Pour the ether extract into a bottle labelled "Ether from Extraction Experiments."

(B) Place the second portion of the original acetic acid solution in a clean 100–150-cc. separatory funnel and extract with 50 cc. of ether as described in part (A). Separate the aqueous layer and extract it a second time, with a fresh portion of 50 cc. of ether. Separate the aqueous layer and extract it a third time, with a fresh portion of 50 cc. of ether. After the third extraction, draw off the aqueous layer into a clean Erlenmeyer flask and titrate with the same standard sodium hydroxide solution (about 1–N) which was used in part (A). Calculate (a) the amount of acetic acid left in the water layer, (b) the amount extracted by the ether, (c) the percentage of the acetic acid left in the water, (d) the percentage extracted by the ether.

Compare the effectiveness of extraction with 150 cc. of ether by the two different procedures.

Pour all the ether extracts into a bottle labelled "Ether from Extraction Experiments."

➔ **Caution:** In the manipulation of organic solvents in a separatory funnel, it is important that the stopcock should be kept properly greased in order to avoid sticking, since the organic solvent removes the stopcock grease. After using an organic solvent in the separatory funnel, it is advisable to clean the separatory funnel thoroughly and to grease the stopcock properly before replacing the apparatus in the laboratory desk. If this is not done, the stopcock is likely to become "frozen" in a fixed position and the separatory funnel will be rendered useless.

QUESTIONS

1. What conclusions can you draw in regard to the most efficient method of extracting acetic acid from an aqueous solution by means of an immiscible solvent?
2. What properties do you look for in a good solvent for extraction?
3. What is meant by the term distribution-coefficient?
4. Explain the fact that acetic acid can be extracted quantitatively from an ether solution by dil. aqueous sodium hydroxide solution.

SALTING-OUT EFFECT

An important fact which is made use of in isolating organic substances from aqueous solutions is that the solubility of many organic substances in water is markedly decreased by the presence of dissolved inorganic salts. For example, ethyl alcohol, which is perfectly miscible with pure water, is only slightly soluble in strong aqueous solutions of sodium chloride, potassium carbonate, and certain other inorganic salts. The same is true of acetone, pyridine, methyl alcohol, and many other water-soluble organic compounds. An explanation which may be suggested to account for this behavior is that the inorganic salts yield ions which are heavily hydrated in the solution, and in consequence there is less *free* water in solutions of these salts.

In the case of solutions of ionized organic substances, such as metallic salts of organic acids and salts of organic bases with mineral acids, it is possible that the *common-ion effect* may also act to decrease the solubility of the salt. Thus, sodium benzenesulfonate is quite soluble in water but is precipitated from an aqueous solution by adding sodium chloride; aniline hydrochloride is readily soluble in water but is only slightly soluble in strong hydrochloric acid solutions.

DRYING AGENTS

The removal of admixed or dissolved water from starting materials and finished preparations is an important feature of organic laboratory work. In general water must be regarded as an objectionable impurity since it may bring about an undesired hydrolytic reaction or exert an unfavorable catalytic effect. The presence of water sometimes retards a desired reaction and may inhibit it completely, as in the formation of Grignard reagents. On the other hand, it would be superfluous to remove the last traces of water from a substance which is to be brought into contact with aqueous reagents.

An organic solid may be dried by spreading it in thin layers exposed to the air at room temperature, but this method usually allows at least a small amount of moisture to remain. More effective drying is obtained by heating the substance in thin layers in a drying oven at a temperature below the melting or decomposition point, or by placing in a desiccator over drying agents such as concd. sulfuric acid, anhydrous calcium chloride, solid sodium hydroxide, etc.

An organic liquid, or an organic solid dissolved in an organic solvent, is usually dried by placing the liquid in direct contact with a solid inorganic drying agent. The selection of an appropriate drying agent involves consideration of the properties of the substance to be dried, and the characteristics of the various drying agents. The latter must remove water efficiently and must not dissolve in the liquid or react with it in any way.

The efficiency of a drying agent refers to the completeness with which it can remove water, and depends essentially on the amount of water existing in equilibrium with the hydration product of the drying agent under the conditions used. Drying capacity relates to the amount of water which can be withdrawn (by hydration or chemical reaction) by a given weight of the drying agent under the conditions used. For example, magnesium sulfate is an efficient drying agent because the vapor pressure of water in equilibrium with its product of hydration ($MgSO_4, 7H_2O$) is quite low at ordinary temperatures; it has an exceedingly high drying capacity since the anhydrous salt can take up 105 per cent of water by weight to form the heptahydrate. Often it is advantageous to eliminate a large part of the admixed water by means of a drying agent of high capacity (calcium chloride, magnesium sulfate) and then complete the drying with a more efficient agent.

The most efficient drying agents remove water by chemical reaction (sodium metal, phosphorus pentoxide, quicklime, etc.) and it is not essential nor always desirable to remove the spent drying agent before distilling the dried liquid. Many drying agents (calcium chloride, magnesium sulfate, sodium hydroxide, etc.) remove water by the formation of hydrates. Since the hydrates generally liberate water when heated, even at moderate temperatures, it is always desirable and usually necessary to remove the spent drying agent before distilling the dried liquid. The most common drying agents are listed below, together with information concerning their properties. Table VII indicates drying agents that are suitable for various classes of organic compounds.

TABLE VII

COMMON DRYING AGENTS FOR ORGANIC COMPOUNDS

Ethers Hydrocarbons	Anhydrous calcium chloride or sulfate, sodium (metal), phosphorus pentoxide
Alcohols	Anhydrous potassium carbonate, anhydrous sulfates (*not* calcium chloride), quicklime
Organic Bases (Amines)	Solid sodium hydroxide or potassium hydroxide, quicklime
Organic Acids	Anhydrous magnesium sulfate, sodium sulfate, calcium sulfate
Alkyl Halides Aryl Halides	Anhydrous calcium chloride, anhydrous sulfates, phosphorus pentoxide
Aldehydes	Anhydrous magnesium sulfate, calcium sulfate, sodium sulfate
Ketones	Anhydrous potassium carbonate, anhydrous sulfates

Anhydrous calcium chloride is widely used because of its high drying capacity and cheapness. It is moderately efficient but not very rapid in action, consequently it should remain in contact with the liquid for an ample time, with occasional shaking.[1] Fused calcium chloride, crushed into small pieces, is more satisfactory than the porous form used for desiccators since the latter tends to retain mechanically an appreciable quantity of liquid.

Alcohols and amines cannot be dried with calcium chloride since they react with it to form molecular compounds analogous to hydrates. Certain aldehydes, ketones, acids, amides and esters also form loose complexes with calcium chloride, but this tendency is greatly reduced if an organic solvent is present. It is inadvisable to use calcium chloride for drying acidic substances (acids, phenols) since the technical product often contains small amounts of basic salts.

Anhydrous magnesium sulfate [2] has a large drying capacity and is rapid and efficient. It is insoluble and chemically inert, and can therefore be used for almost all types of organic compounds. Anhydrous sodium sulfate is equally inert but is slower and much less efficient.

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[1] If in any drying operation sufficient water is present to cause the separation of an aqueous layer, the organic liquid should be decanted and treated with a fresh portion of the drying agent.

[2] The anhydrous salt can be prepared readily by heating Epsom salts ($MgSO_4 \cdot 7H_2O$) to dryness in a porcelain dish or casserole over a wire-gauze, and stirring with a spatula or glass rod until a dry powder is obtained.

Anhydrous calcium sulfate in a form suitable for drying purposes has been introduced under the trade name *Drierite*.[1] This reagent is extremely rapid and efficient, is chemically inert, and insoluble in organic liquids. When a large amount of water must be removed it is good practice to use a preliminary drier of larger capacity (magnesium sulfate, calcium chloride, etc.) since *Drierite* takes up only 6.6 per cent by weight of water, forming the hydrate $CaSO_4,\frac{1}{2}H_2O$.

Anhydrous potassium carbonate may be used for drying neutral and basic compounds (alcohols, ketones, esters, nitriles, amines, etc.) but not for acids or phenols. It has good drying capacity but is rather slow and only moderately efficient. It is used frequently in salting out water-soluble alcohols, amines, and ketones from aqueous solutions, and as a preliminary drier.

Solid sodium hydroxide and *potassium hydroxide* are rapid and effective drying agents for organic bases (amines). Their use is quite restricted since they react with many organic compounds in the presence of water and are soluble in certain organic liquids. Technical flake sodium hydroxide (ordinary solid household lye, in small cans) is convenient and inexpensive.

Calcium oxide (*quicklime*) is a slow but efficient drying agent, which acts by chemical combination. The oxide and resulting hydroxide are stable to heat and practically non-volatile, consequently the spent drying agent need not be removed. It is used frequently for drying low molecular weight alcohols and amines, but cannot be used for acidic or alkali-sensitive substances.

Sodium (*metal*) is most effective in the form of fine wire, which is forced directly into the liquid by means of a sodium press. Sodium removes water very efficiently but is so active chemically that its use is restricted to the most inert types of compounds (saturated and aromatic hydrocarbons, and ethers). A preliminary drying should always be carried out before using sodium.

Sodium must be manipulated with great care, and used only in small amounts. The metal is stored under a hydrocarbon oil (kerosene or xylene) to prevent reaction with air and moisture. Sodium should not be handled with the fingers but with tongs or pincers. Waste or residual pieces of sodium must never be thrown into a waste jar or sink, and should not be destroyed by throwing them into water. Sodium residues should be placed under kerosene in a bottle provided for this purpose.

Phosphorus pentoxide is exceedingly efficient and rapid; it combines chemically with water to give HPO_3 and finally H_3PO_4. It can be used for drying hydrocarbons, ethers, alkyl and aryl halides, esters and nitriles, but reacts with most other compounds. Since phosphorus pentoxide is relatively expensive and is difficult to handle (causing severe burns on the skin), it is used only when extreme dryness is required and should always be preceded by a preliminary drying agent.

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[1] *Drierite* must not be confused with *Dehydrite* (magnesium perchlorate). Although *Dehydrite* and *Desicchlora* (barium perchlorate) are excellent drying agents for certain purposes, they should not be used for organic materials owing to the danger of violent explosions.

In many cases it is possible to apply the principle of steam-distillation for drying organic liquids and solids. For example, if wet benzene or a wet benzene solution of an organic substance is subjected to distillation, the first portion of the distillate consists of a mixture of benzene and water. This mixture distils at a temperature below the boiling-point of benzene (80°); when the water has been removed benzene distils, and finally the pure dry organic liquid (or solid) remains. This method is very simple and very useful for drying many organic substances; occasionally carbon tetrachloride, toluene, xylene, and other water-insoluble liquids are used in place of benzene.

In certain instances, especially with the simpler aliphatic alcohols, drying by distillation with benzene is complicated by the formation of a ternary azeotropic mixture of benzene-water-alcohol, and a binary azeotropic mixture of benzene-alcohol. In such cases the amount of benzene used must be carefully controlled to avoid a large excess.

The commercial use of distillation with benzene to prepare absolute ethyl alcohol from the constant-boiling (azeotropic) mixture of ethyl alcohol and water is an example of the latter type. The ternary azeotropic mixture, benzene-water-ethyl alcohol, boils at 64.85° and contains 74.1 per cent by weight of benzene, 7.4 per cent of water, and 18.5 per cent of ethyl alcohol. When the water has been removed, a binary azeotropic mixture, containing 67.63 per cent by weight of benzene and 32.37 per cent of ethyl alcohol, distils at 68.24°. When the benzene has been removed, the residue consists of practically pure absolute ethyl alcohol which distils at 78.3°.

Experiment 7

SALTING-OUT EFFECT
DRYING AGENTS

In a 500-cc. separatory funnel, place 60 cc. of *n*-butyl alcohol (butanol-1) and add 300 cc. of pure water. Shake the mixture thoroughly for two or three minutes and allow the layers to separate. Draw off the lower aqueous layer and collect it in a large flask. Pour off the *n*-butyl alcohol through the mouth of the funnel (Why?) and measure its volume. From the contraction in volume estimate roughly the solubility of *n*-butyl alcohol in water at room temperature.

Salting-Out Effect. To the aqueous layer add enough clean salt (sodium chloride) to saturate the solution (about 30 g. will be required for every 100 cc.) and shake thoroughly until no more salt will dissolve. Decant the liquid from any excess of salt into the separatory funnel and allow the layers to separate. Draw off and discard the salt solution. Pour off the *n*-butyl alcohol through the mouth of the funnel and measure its volume.

Combine the two portions of *n*-butyl alcohol in a small dry flask, mix thoroughly and measure the total volume. Calculate the percentage of the recovered *n*-butyl alcohol which was obtained by salting-out the aqueous solution. Reserve the recovered wet *n*-butyl alcohol for drying experiments.

In practice the wet organic liquid obtained in the preceding paragraph would be dried with a suitable drying agent and purified by distillation. For this experiment, however, in order to show the effects of drying, the sample is divided into two portions and only one of these is dried.

Drying Agents. (A) Place one-half of the wet *n*-butyl alcohol in a small distilling flask, add a few chips of clay plate, and distil on an asbestos-centered wire-gauze (as described in Exp. 3). Record the boiling-point range. Pour the distilled *n*-butyl alcohol into the bottle on the side-shelf, labelled "Wet *n*-Butyl Alcohol."

(B) Place the second half of the wet *n*-butyl alcohol in a small dry distilling flask and add 16–18 g. of *fresh* quicklime as a drying

agent. Cork the flask and close the side-tube with a short rubber tube holding a plug of solid glass rod. Allow to stand overnight and observe.

Add a few small chips of clay plate and distil on an asbestos-centered wire-gauze (as described in Exp. 3). Record the boiling-point range, and compare with the result obtained when the wet *n*-butyl alcohol was distilled. Pour the distilled *n*-butyl alcohol into the bottle on the side-shelf, labelled "Dried *n*-Butyl Alcohol."

(C) In a 250–300-cc. separatory funnel, place 20 cc. of carbon tetrachloride and add about 150 cc. of pure water. Shake the mixture thoroughly and allow the layers to separate. Draw off the lower layer of carbon tetrachloride and measure its volume. From this result estimate roughly the solubility of carbon tetrachloride in water, and compare with that of *n*-butyl alcohol.

Place the recovered carbon tetrachloride in a small dry Erlenmeyer flask and add 5–6 g. of anhydrous calcium chloride or of Drierite, as a drying agent. The liquid should be allowed to stand in contact with calcium chloride, with occasional shaking, for at least thirty minutes in order to obtain satisfactory drying; ten minutes is sufficient for Drierite.

Through a funnel containing a small plug of cotton (or a small fluted filter), decant the dried liquid into a dry distilling flask of the proper size. Add a few small chips of clay plate and distil on an asbestos-centered wire-gauze. Record the boiling-point range and compare with the value given in one of the chemical handbooks. Pour the distilled carbon tetrachloride into the bottle provided on the side-shelf, labelled "Dried Carbon Tetrachloride."

QUESTIONS

1. In drying *n*-butyl alcohol could you have used: calcium chloride? anhydrous sodium sulfate? anhydrous potassium carbonate? phosphorus pentoxide?
2. In drying carbon tetrachloride could you have used: quicklime? phosphorus pentoxide? metallic sodium?
3. After drying carbon tetrachloride with anhydrous calcium chloride, why is it necessary to remove the used drying agent before distilling the dried material?
4. What quantity of each of the following drying agents would be required to combine with 2 g. of water: quicklime? metallic sodium? Drierite? magnesium sulfate? calcium chloride (assuming formation of the tetrahydrate)?

QUALITATIVE DETECTION OF ELEMENTS

Carbon, Hydrogen, Oxygen. The elements which are most commonly present in organic compounds are carbon, hydrogen, and oxygen. The presence of carbon and hydrogen may be detected qualitatively by heating the substance in a tube with dry powdered copper oxide, whereby carbon dioxide and water are formed. Carbon is detected by passing the evolved gases into an aqueous solution of calcium or barium hydroxide, whereupon the carbon dioxide produces a precipitate of the carbonate. Hydrogen is detected by the condensation of droplets of water in the cool upper portion of the reaction tube.

There is no satisfactory qualitative test for the presence of oxygen in organic compounds. In order to determine whether or not oxygen is present, it is necessary to have recourse to quantitative analysis. If the sum of the percentages of all the constituent elements does not amount to 100 per cent, the deficit is taken as the percentage of oxygen.

Nitrogen, Halogens, Sulfur. The qualitative detection of these elements in organic compounds is more difficult than in inorganic compounds on account of the fact that most organic compounds are not appreciably ionized in solution. Since the common tests used in qualitative inorganic analysis depend upon ionic reactions, they cannot be applied directly to organic compounds. For example, sodium chloride or bromide gives an immediate precipitate of the silver halide when treated with an aqueous solution of silver nitrate; carbon tetrachloride, carbon tetrabromide, and most organic halides, do not produce a precipitate of the silver halide when treated with aqueous silver nitrate solution. These organic halides fail to respond to the common test for halides because they do not furnish an appreciable amount of halide ions in the solution.

For qualitative detection it is necessary, therefore, to convert elements such as nitrogen, sulfur, and halogens into ionized inorganic substances in order to apply suitable tests. This conversion may be accomplished by several methods, of which the most general is that of fusion with metallic sodium. In this way there are formed sodium cyanide, sodium halides, sodium sulfide, etc., as indicated below. The resulting ionized compounds may then be detected by applying the usual inorganic tests:

Organic compound containing C H O N S Cl

$$+ \text{Na} \xrightarrow[\text{temperature}]{\text{high}} \text{NaCN} + \text{NaCl} + \text{Na}_2\text{S} + \text{NaOH} + \text{etc.}$$

Nitrogen. The filtered alkaline solution is treated with aqueous ferrous sulfate and ferric chloride, boiled for a few moments and acidified with hydrochloric acid. If nitrogen is present, a precipitate of prussian blue results:

$$2\text{NaCN} + \text{FeSO}_4 \longrightarrow \text{Fe(CN)}_2 + \text{Na}_2\text{SO}_4$$
$$4\text{NaCN} + \text{Fe(CN)}_2 \longrightarrow \text{Na}_4\text{Fe(CN)}_6$$
$$3\text{Na}_4\text{Fe(CN)}_6 + 4\text{FeCl}_3 \longrightarrow \underset{\text{(prussian blue)}}{\text{Fe}_4[\text{Fe(CN)}_6]_3} + 12\text{NaCl}$$

Sulfur. A fresh portion of the filtered alkaline solution is acidified with acetic acid and treated with an aqueous solution of lead acetate. If sulfur is present, a dark brown precipitate of lead sulfide results.

Sulfur may also be detected by the use of a solution of sodium nitroprusside, which gives a deep reddish-violet coloration with solutions of sulfides. The following equation has been given for the reaction:

$$\text{Na}_2\text{S} + \text{Na}_2\text{Fe(CN)}_5\text{NO} \longrightarrow \text{Na}_4\text{Fe(CN)}_5\text{S} + \text{NO}$$

Halogens. A fresh portion of the filtered alkaline solution is acidified with nitric acid and boiled for a short while in order to expel hydrogen cyanide and hydrogen sulfide (if nitrogen and sulfur are present). The resulting solution, which contains free nitric acid, is treated with aqueous silver nitrate, and if halogens are present a precipitate of silver halide results. The usual qualitative methods are employed in testing for the individual halogens, or in detecting two or more halogens in the presence of each other.

In place of the sodium-fusion method, certain other methods may be used for the conversion of the elements into ionized inorganic substances. For the detection of halogens, heating with pure calcium oxide (quicklime) is sometimes employed. By this means the calcium halides are produced and can be detected in the usual way. Fusion with sodium peroxide in the Parr peroxide bomb[1] is a very useful and generally applicable method for the qualitative and quantitative determination of carbon, halogens, sulfur, phosphorus, etc., in organic substances.

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[1] For a detailed description of the use of the Parr peroxide bomb, consult W. A. Noyes, *Organic Chemistry for the Laboratory*, fifth edition, pages 9–14, 28–31, The Chemical Publishing Co., Easton, Pa. (1926), or H. L. Fisher, *Laboratory Manual of Organic Chemistry*, fourth edition, pages 384–388, John Wiley and Sons, Inc., New York (1938).

Experiment 8

QUALITATIVE DETECTION OF ELEMENTS

Carbon. Heat a small amount of sugar (sucrose, $C_{12}H_{22}O_{11}$) on a crucible cover. Notice that inflammable gases are evolved, leaving a charred residue of carbon.

Carbon and Hydrogen. In a porcelain crucible, place 1–2 g. of finely powdered cupric oxide and dry by heating for a few minutes with a Bunsen flame. While the copper oxide is still warm, carefully mix it with about one-tenth of its bulk of powdered sugar and place the mixture in a hard glass test-tube fitted with a cork and right-angled delivery tube. Arrange the delivery tube so that the gases evolved are passed into about 5 cc. of limewater (calcium hydroxide solution) in a test-tube. Heat the mixture of copper oxide and sugar, and observe the result. Note the water which condenses in the cool portion of the tube. Remove the delivery tube from the limewater before allowing the copper oxide to cool (Why?).

Halogens. (A) *Beilstein's Test.* Heat a copper wire spiral to redness until the flame is no longer colored. Cool, moisten the spiral with about two drops of carbon tetrachloride (CCl_4), heat again and observe. The color is given to the flame by the vapor of the copper halide formed.

(B) *Calcium Oxide Test.* In a test-tube heat a small lump of pure quicklime (halogen free) to a high temperature, and while still hot add about two drops of carbon tetrachloride (CCl_4). When cold, boil with 5–10 cc. of distilled water, transfer to a 100-cc. beaker and dissolve in dil. nitric acid (1 vol. of concd. nitric acid to 1 vol. of distilled water). If a clear solution is not obtained, filter the solution before proceeding. Add 2–3 cc. of a dil. solution of silver nitrate (5–10 per cent) and observe.

Sulfur. *Carius' Test.* In a large test-tube, warm a very *small amount* (about 0.5 g.) of sulfanilic acid ($NH_2C_6H_4SO_3H$) with 5 cc. of concd. nitric acid until the reaction begins; then discontinue the heating or the oxidation will become too violent. When the reaction is complete, dilute with about 25 cc. of distilled water and

add 5–10 cc. of a solution of barium chloride (5–10 per cent). The precipitation of barium sulfate indicates that the sulfur has been oxidized to sulfuric acid. Carius' test cannot be used for those sulfur compounds which will not decompose with nitric acid.

➔**Caution:** In this oxidation proceed with care and do not use larger amounts of materials than those specified.

Sodium Fusion Method. Support a small test-tube (about 50 mm. × 8 mm.) in a clamp, or insert the tube through a small hole in a piece of asbestos board so that the tube is supported by its rim. Drop in a piece of bright sodium (metal) no larger than a small pea, and heat until the sodium melts and its vapors fill the lower part of the tube. Remove the flame momentarily, and add suddenly a halogen, sulfur, or nitrogen compound (if a mixture of sulfanilic acid and *p*-dichlorobenzene is used, it is possible to make all three tests from one fusion). If a solid, use only a small pinch of the material; if a liquid, use only a few drops. A spontaneous exothermic reaction takes place. Return the flame and heat the tube to redness. Insert the tube through a circular piece of asbestos paper, large enough to act as a cover to a small beaker, and while the tube is still hot touch the bottom of the tube to the surface of about 15 cc. of distilled water contained in the beaker. The tube will usually crack and the water will then react more or less violently with the excess of sodium. When the reaction subsides, crush the end of the tube in the beaker, and then heat to boiling on an asbestos-centered wire-gauze. Filter through a small filter paper and apply one or all of the following tests to the solution.

➔**Caution:** Carry out the sodium fusion with care, and be especially cautious in decomposing the fused mass with water. If too large an amount of sodium is used, the treatment with water may result in a small explosion.

Metallic sodium must be manipulated with great care. Never use large quantities of metallic sodium and do not touch the sodium with your fingers—use tongs or pincers. Do not throw small residual pieces of sodium into water, or into a sink or waste crock; place sodium residues in the bottle provided for this purpose.

(A) *Nitrogen.* To a portion of the solution add five drops of a freshly prepared ferrous sulfate solution, one drop of ferric chloride solution, and then enough sodium hydroxide solution (usually

1–2 cc. of a 10 per cent solution) to produce a distinct alkalinity. Heat to boiling, cool, and acidify with dil. hydrochloric acid. A precipitate of prussian blue, indicating the presence of nitrogen, may be detected after standing for a short time, by filtering through a small filter.

It is reported that the addition of a very small amount of potassium fluoride is effective in bringing about precipitation of the prussian blue.

Since the presence of sulfur often obscures the nitrogen test, it is advisable, when sulfur is present, to modify the procedure in the following way: To a portion of the solution add five drops of freshly prepared ferrous sulfate solution and enough sodium hydroxide to produce a distinct alkalinity (usually 1–2 cc. of a 10 per cent solution). Heat to boiling and filter from the precipitate of iron sulfide. Acidify with dil. hydrochloric acid, and add a drop of ferric chloride solution to obtain the precipitate of prussian blue.

(B) *Sulfur.* Acidify a portion of the solution with acetic acid, boil, and test the evolved gases for hydrogen sulfide with a strip of filter paper moistened with lead acetate solution. To another portion of the solution add 1–2 drops of a solution of sodium nitroprusside. A deep coloration indicates sulfur.

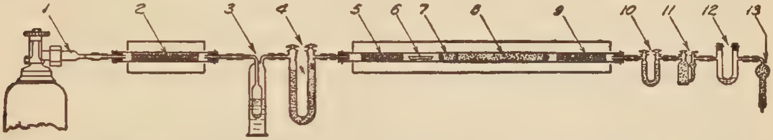
(C) *Halogens.* Acidify the remainder of the solution with dil. nitric acid (1 vol. of concd. nitric acid to 1 vol. of water) and boil gently for five or ten minutes to remove any hydrogen cyanide which may have been formed. Add about 5 cc. of a dil. solution of silver nitrate (5–10 per cent) and continue the gentle boiling for a few minutes. A heavy precipitate indicates the presence of halogen; if there is only a faint turbidity, it is probably due to the presence of impurities in the reagents.

QUESTIONS

1. Why do most organic halogen compounds, before treatment with lime, give no precipitate with silver nitrate solution?
2. What is the meaning of the word "halogen" and why is it applied to chlorine, bromine, and iodine?
3. By what fault in the procedure might a compound which contains nitrogen but not halogen, be found to give a positive test for halogen?
4. What important class of foods contains nitrogen?
5. What tissues of the body are especially rich in sulfur?

QUANTITATIVE ORGANIC ANALYSIS[1]

Carbon and Hydrogen. The quantitative determination of carbon and hydrogen in organic compounds is effected by combustion of the substance in an atmosphere of purified air or oxygen, and weighing the resulting water and carbon dioxide by absorption in suitable reagents (the method of Liebig). For this purpose the combustion is carried out in a glass tube packed with copper oxide, which is maintained at a high temperature to insure complete oxidation of the organic matter. The gases from the combustion tube are passed through an absorption train which consists of a tube containing a water absorbent, a tube containing a carbon dioxide absorbent, and a safety tube containing an additional quantity of the carbon dioxide and water absorbents. The increases in weight of the first and second absorption tubes give the weights of water and carbon dioxide respectively, and from these data and the weight of the original substance the percentages of hydrogen and carbon may be calculated.



1. Needle valve for reducing and controlling pressure of oxygen. 2. Copper oxide preheater, to oxidize traces of hydrogen-containing compounds. 3. Sulfuric acid wash bottle to remove water from the oxygen. 4. Absorption tube to remove carbon dioxide from the oxygen. 5. Copper oxide spiral. 6. Boat for sample to be analyzed. 7. Cerium oxide catalyst. 8. Copper oxide wire. 9. Reduced copper spiral to reduce oxides of nitrogen. 10. Absorption tube for water. 11. Absorption tube for carbon dioxide. 12. Sulfuric acid bubbler. 13. Safety tube to remove moisture and carbon dioxide from air which might be drawn back into the apparatus.

FIG. 16.—Organic Combustion Apparatus.

For the absorption of water the common absorbents are concd. sulfuric acid (usually in the form of pumice stone soaked in the reagent), magnesium perchlorate trihydrate (Dehydrite) and alumina. Anhydrous calcium chloride is not often employed, since the commercial product often contains basic salts which absorb carbon dioxide and consequently give high results for hydrogen and low results for carbon.

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[1] An excellent discussion of organic combustion analyses is given in H. L. Fisher, *Laboratory Manual of Organic Chemistry*, fourth edition, pages 283–388, John Wiley and Sons, Inc., New York (1938).

A variety of reagents may be used for the absorption of carbon dioxide. Until rather recently a strong aqueous solution of potassium hydroxide was most commonly used. Solutions of sodium hydroxide and of barium hydroxide have been employed to some extent. A recently developed absorbent for carbon dioxide, which is more satisfactory than the above aqueous solutions, is a porous solid mixture of sodium hydroxide and asbestos (Ascarite).

Carbon (but not hydrogen) may be determined by fusion with sodium peroxide in the Parr peroxide bomb. The fused mass containing the resulting sodium carbonate is dissolved in water and treated with hydrochloric acid in a suitable apparatus. The volume of carbon dioxide produced is then measured by the usual gasometric methods.

Oxygen. Since there is no simple qualitative or quantitative method for the determination of oxygen in organic compounds, the presence and the amount of this element are usually found by determining all of the other elements which are present and assuming the deficit to be oxygen.

For certain classes of compounds oxygen may be determined directly by means of catalytic hydrogenation in the presence of nickel; the carbon is converted to methane, and the oxygen into water which is determined by absorption in a suitable reagent in the usual way.[1]

Another method for the determination of oxygen depends upon the gasometric determination of the amount of molecular oxygen consumed during the combustion of the organic compound to form carbon dioxide and water. In this method the combustion is effected in the presence of platinized asbestos in a closed system, and the carbon, hydrogen, and oxygen are determined in a single operation.[2]

Nitrogen. The most general method for the quantitative determination of nitrogen is the Dumas method, which consists of effecting combustion of the organic substance in an atmosphere of carbon dioxide and determining the volume of gaseous nitrogen produced. For this purpose the combustion is carried out in a tube packed with copper oxide and containing a gauze of metallic copper (to reduce oxides of nitrogen to free nitrogen). The gaseous nitrogen is collected over a strong solution of potassium hydroxide (which serves to remove carbon dioxide and water) and its volume is carefully measured at a definite temperature and pressure. From these data the weight of nitrogen may readily be obtained.

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[1] H. ter Meulen and J. Heslinga, *Neue Methoden der Organisch-Chemischen Analyse;* Akademische Verlagsgesellschaft m.b.H., Leipzig (1927).

[2] Glockler and Roberts, *J. Am. Chem. Soc.*, **50**, 828 (1928).

Nitrogen in the form of amino groups may be determined conveniently by the Kjeldahl method. The organic substance is digested with concd. sulfuric acid and potassium sulfate (in the presence of a small amount of cupric or mercuric sulfate) and the amino nitrogen is converted to ammonium sulfate. The ammonia is then liberated by the addition of alkali and distilled into an excess of standard acid solution. The excess of standard acid is determined by titration with standard alkali, and the quantity of nitrogen may then be calculated from the amount of acid which is required to neutralize the ammonia produced.

Compounds containing nitrogen in the form of nitro groups, azo groups, and other reducible forms may be converted by preliminary reduction to amino compounds, and the nitrogen may then be determined by the Kjeldahl method.

Halogens, Sulfur, etc. The only special feature of the quantitative determination of these elements in organic compounds is the necessity of a preliminary decomposition to form ionized substances. When this decomposition has been effected, the usual quantitative methods, gravimetric and volumetric, may be employed.

Several of the common methods of decomposition (heating with calcium oxide, fusion with sodium peroxide, etc.) have already been mentioned in connection with the qualitative detection of these elements. In addition, there is the method of Carius, which consists in heating the substance in a sealed tube with fuming nitric acid.

The Preparation and Reactions of Typical Organic Compounds

GENERAL REMARKS

In performing experiments the student should bear in mind that the preparations and reactions studied for a particular compound are usually examples of methods and reactions which can be applied to an entire class of compounds (often to entire homologous series). After the completion of an experiment it is well for the student to consider the general utility and the limitations of the method of preparation which was used, and of any reactions or tests which were performed. The generalizations should be as far reaching as possible, but must be considered carefully or they may be made too wide.

In many experiments a definite product is prepared and purified. The preparation thus obtained should be placed in an appropriate bottle (wide-mouth bottles for solids and narrow-mouth bottles for liquids) of suitable size, labelled with the information given below, and presented with the notebook and report card when the experiment is submitted for final approval.

LABELS FOR PREPARATION BOTTLES

Name of product prepared	Amylene (Pentene-2)
M.P. or B.P. as actually observed	B.P. 35–41°
Student's name	R. C. Taylor
Actual yield (in g.)	Yield 12 g. Tare, 37.5 g.
Tare of bottle (with stopper or cork)	

The purity of the preparation and the general appearance of the preparation bottle serve as an index of the neatness and skill of the student in laboratory manipulations. Preparations should not be submitted in flasks, test-tubes, etc., but in clean dry bottles or specimen tubes (for very small quantities) which are fitted with glass stoppers or *clean corks of the proper size.*[1] The use of dirty corks or bottles, and of glass stoppers or corks which do not fit the container properly, is an indication of carelessness and poor laboratory technic. Rubber stoppers should never be used for preparation bottles.

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[1] For the preparation bottle, the cork should be selected of such size that it will extend from one-third to one-half of its length (but not farther) into the mouth of the bottle.

It is often advantageous to collect the purified preparation directly in a dry bottle, previously weighed together with the stopper or cork. The weight of the empty bottle with its stopper or cork is called the tare. This weight should be recorded in the laboratory notebook and on the label of the bottle.

For liquid preparations the observed boiling-point should be recorded directly in the laboratory notebook, and copied on the label and the report card. For solids (except certain very high-melting substances), the melting-point should be determined and recorded directly in the notebook, and copied on the label and the report card.

THE CALCULATION OF YIELDS

The yield (sometimes called the actual yield) is the amount of the pure product which is actually obtained in the experiment. The theoretical yield (sometimes called the calculated yield) is the amount which could be obtained under theoretically perfect or ideal conditions; that is, if the main reaction proceeded perfectly to completion and no side reactions or mechanical losses occurred, so that the starting materials were entirely converted into the desired product and no material was lost in isolation and purification.

The percentage yield is obtained by comparing the actual yield with the theoretical yield, in the following manner:

$$\text{Percentage yield} = \frac{\text{actual yield}}{\text{theoretical yield}} \times 100$$

The percentage yield is the measure of the over-all efficiency of the preparation, since all the variable factors such as incomplete reactions, side reactions, and mechanical losses affect the actual yield. In elementary laboratory work it is usually considered just as important to obtain a pure product as to obtain a satisfactory yield. The student may be required to repeat a preparation unless a certain minimum yield is attained, in order to emphasize the development of skill and care in manipulation and in following laboratory directions. Nevertheless, the student must not sacrifice the purity of the product to the obtainment of a larger quantity of the product in an impure state.

In actual laboratory work, the best results are not always obtained by using the reagents in the exact proportions which are indicated in the equation for the reaction. In some cases it is advisable to use the reacting materials in the exact proportions demanded by the equation, but in many cases it is better to use an excess of one of the reacting materials. In a given preparation the choice depends upon a number of factors, and the student is expected to determine why the particular proportion of reagents is used. If a preparation involves two reacting substances and the amounts actually used are not in the exact proportions demanded by the equation, it is necessary to determine by calculation which of the reactants is the limiting factor for the calculation of the theoretical yield. The theoretical yield is based upon the reactant which is the limiting factor, as shown by the example given below. In this connection the terms *mole* and *moles used* are commonly employed. A *mole* is a gram-molecule, and is equal to the molecular weight expressed in grams.[1] The term *moles used* is employed to express the number of moles or the fraction of a mole of a particular compound actually used in an experiment. The number of moles is equal to the weight of the substance divided by the molecular weight.

THEORETICAL AND PERCENTAGE YIELDS

Suppose that methyl ethyl ether, $CH_3—O—C_2H_5$, has been prepared by the action of methyl iodide upon sodium ethoxide (the Williamson synthesis of ethers). This preparation is carried out by reacting metallic sodium with ethyl alcohol and treating the resulting sodium ethoxide with methyl iodide:

$$\text{(a)}\quad C_2H_5\text{—}OH + Na \longrightarrow C_2H_5\text{—}ONa + \tfrac{1}{2}H_2$$

$$\text{(b)}\quad C_2H_5\text{—}ONa + CH_3\text{—}I \longrightarrow C_2H_5\text{—}O\text{—}CH_3 + NaI$$

The equations (a) and (b) may be summarized as follows:

$$\begin{array}{l} \text{(c)}\quad C_2H_5\text{—}OH + Na + CH_3\text{—}I \longrightarrow C_2H_5\text{—}O\text{—}CH_3 + NaI + \tfrac{1}{2}H_2 \\ \qquad \text{1 mole : 1 mole : 1 mole} \longrightarrow \quad \text{1 mole} \;:\; \text{1 mole} : \tfrac{1}{2}\text{ mole} \end{array}$$

---

[1] The term mole is used most frequently in indicating the proportions of various reagents, and any convenient weight unit might be chosen. For laboratory purposes the gram is most convenient and is chosen for that reason. For some purposes the unit weight is taken as a kilogram or a milligram, and the terms kilogram-mole or millimole are used. Obviously, a kilogram-mole is equal to 1000 gram-moles, and a millimole is equal to 0.001 gram-mole.

From this it can be seen that the proportions demanded by the equation are 1 mole of $C_2H_5—OH$: 1 mole of Na : 1 mole of $CH_3—I$, and the resulting products would be 1 mole of $C_2H_5—O—CH_3$: 1 mole of NaI : $\frac{1}{2}$ mole of H_2.

Suppose that the following quantities of the reagents are actually used in a laboratory preparation:

$$\begin{aligned}
&\text{92.0 g. of absolute ethyl alcohol} &&= \frac{92}{46}\text{ moles} &&= 2.0\text{ moles } C_2H_5—OH\\
&\text{5.5 g. of metallic sodium} &&= \frac{5.5}{23}\text{ mole} &&= 0.24\text{ mole Na}\\
&\text{28.4 g. of methyl iodide} &&= \frac{28.4}{142}\text{ mole} &&= 0.20\text{ mole } CH_3—I
\end{aligned}$$

The amounts of these reagents are then converted from grams into moles (by dividing by the molecular weights), in order to compare them with the molar proportions expressed in the equation. The relative proportions actually used are thus 10 of $C_2H_5—OH$: 1.2 of Na : 1.0 of $CH_3—I$. Obviously, ethyl alcohol and sodium are used in excess, and methyl iodide is the limiting factor which will determine the theoretical yield.

From equation (b) or (c), it can be seen that 1 mole of methyl iodide reacting with a sufficient quantity of sodium ethoxide will produce, under perfect conditions, exactly 1 mole of methyl ethyl ether. Consequently, the maximum amount of methyl ethyl ether which could be produced in the above preparation (the theoretical yield) is 0.2 mole. By multiplying this fraction of a mole by the weight of 1 mole of methyl ethyl ether (60 g.), the theoretical yield is converted into grams. The weight of 1 mole of methyl ethyl ether is the gram-molecular weight; this is determined by multiplying the number of atoms of each element by its atomic weight, and taking the sum of these weights.

$$\begin{aligned}
&C_2H_5—O—CH_3 = C_3H_8O\\
&\text{1 mole} = (3 \times 12 + 8 \times 1.0 + 1 \times 16)\text{ g.} = 60\text{ g.}\\
&\text{Theoretical yield} = 0.2 \times 60\text{ g.} = 12.0\text{ g.}
\end{aligned}$$

If the actual yield of methyl ethyl ether in the above preparation was 8.2 g., the percentage yield would be:

$$\text{Percentage yield} = \frac{8.2}{12.0} \times 100 = 68.3\text{ per cent}$$

Problem. In another preparation of methyl ethyl ether suppose that the amounts of the reagents actually used were: 6.9 g. of metallic sodium, 46 g. of absolute ethyl alcohol, and 49.7 g. of methyl iodide. Calculate the theoretical yield, in grams. (Ans. = 18.0 g.)

Assuming that the actual yield in the above preparation was 15.0 g., calculate the percentage yield. (Ans. = 83.3 per cent.)

NOTEBOOKS [1]

(See also page 3)

In the subsequent experiments on the laboratory preparation and reactions of typical organic compounds, the preparation of the notebook involves several features which were not required for the experiments on laboratory operations. The most important of these is a table of physical constants of the substances which are manipulated in the experiment (see paragraph 4, below). By having this information available the student will be able to understand more readily the reasons for the particular procedure which is followed in the experiment, and will often be able to overcome independently any small difficulties which arise in the course of the experiment. The student is expected to proceed in the following manner:

1. Read the laboratory directions for the entire experiment, note particularly the cautions for handling materials, and try to understand the reasons for the procedure which is followed. It is often helpful to refer to the textbook or lecture notes for a discussion of the particular class of compounds which is to be studied.

2. In the notebook, write a general statement of the main reaction which is to be carried out, and attach the laboratory direction sheet.

3. Write balanced equations, using condensed structural formulas, for the main and side reactions, and for any tests which are carried out.

4. Prepare a table of the physical constants of all organic and inorganic substances which enter into the main and side reactions, and are produced in these reactions. Use the following form:

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[1] The following specific directions for the preparation of notebooks and the general laboratory procedure are those which are used in the elementary courses in organic chemistry at the University of Illinois and at Cornell University. For the particular conditions which obtain in other laboratories the instructor in charge of the laboratory work may wish to alter these directions or substitute others.

TABLE VIII

FORM FOR TABULATING PHYSICAL CONSTANTS

SUBSTANCE	M.W.	GRAMS USED	MOLES USED	SP. G. 20°	M.P.	B.P. (760 MM.)	SOLUBILITY (IN G. PER 100 CC.)		
							Water	Alcohol	Ether
Bromine	160	96	0.6	3.18	−7°	59°	4	sol.	sol.
Benzoic acid. .	122	49	0.4	——	121.2°	24.9°	0.34	57	47
Benzene	78	156	2.0	0.878	5.4°	80–81°	0.07	∞ *	∞

* The infinity sign ∞ is commonly used to designate miscibility in all proportions.

The physical constants of common organic and inorganic compounds may be found in the chemical handbooks.[1] A table of physical constants of the less common organic compounds which are manipulated in the experiments in this laboratory manual is given in the appendix.

5. Calculate the number of moles used (or the fractions of moles) of the reacting substances, and the theoretical yield (in g.).

6. After preparing the notebook in accordance with the foregoing instructions, submit it to the instructor for preliminary approval BEFORE STARTING TO PERFORM THE EXPERIMENT.[2] In certain experiments, the student will be expected to arrange the apparatus for the experiments and secure the approval of the instructor for the set-up.

At the time of the preliminary approval, the instructor will countersign a stockroom order for the required reagents which are not on the laboratory side-shelf, and will issue a report card for the experiment.

7. Perform the experiment *according to the laboratory directions*, and promptly record your observations (including physical con-

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[1] Such as the Chemical Tables from the *Handbook of Chemistry and Physics*, Chemical Rubber Publishing Co., Cleveland, Ohio; Lange's *Handbook of Chemistry*, Handbook Publishers, Inc., Sandusky, Ohio; Van Nostrand's *Chemical Annual; The Chemist's Yearbook*, etc. The most complete and authoritative information on organic compounds is found in Beilstein's monumental work, *Handbuch der Organischen Chemie*, of which the most recent edition comprises about forty large volumes.

[2] If an experiment is performed without preliminary preparation of the notebook and preliminary approval by the instructor, the student may receive only partial credit for the experiment or may be required to repeat the experiment. The laboratory instructors should reserve the first half-hour of each laboratory period for the preliminary approval of notebooks.

stants as actually observed, actual yields, etc.) directly into the notebook. Always observe and record the boiling-point of a liquid preparation, and the melting-point of a solid organic preparation (provided the melting-point is not above 250°).

8. Record the actual yield, and calculate the percentage yield. Record any general conclusions drawn from your performance of the experiment.

9. Write balanced equations illustrating any other important methods of preparing the product, and write answers to the questions given on the direction sheets. In your answers use condensed structural formulas, and make complete statements.

10. Promptly on completion of the experiment, submit the completed notes and the report card, together with any substance prepared, to the instructor for final approval. The instructor will examine the notes and the product prepared, and may ask questions designed to test the student's knowledge of the fundamental principles involved in the experiment, and to test his ability to make generalizations and to apply generalizations to specific cases.

In order to make efficient use of the time assigned for laboratory work, the student is expected to plan his laboratory schedule and to make preliminary preparations before coming to the laboratory.

Since many experiments require that the reagents be refluxed for several hours, the student should plan to perform other laboratory work while the operation of refluxing is being carried out. To aid the student in planning his schedule, the time required for refluxing or for allowing materials to stand is noted in the appendix.

Experiment 9

REACTIONS OF SATURATED HYDROCARBONS THE METHANE SERIES

The following tests should be carried out in clean, dry test-tubes. Record the results of the three series of experiments in tabular form in your notebook (see page 105).

Purified Gasoline.[1] Perform the following tests with a sample of purified gasoline:

(A) Add 1–2 cc. of the purified gasoline to each of two portions of 3–4 cc. of bromine water. Shake well and observe after two or three minutes. Place one tube in your laboratory locker and place the second tube in bright sunlight. Allow both tubes to stand for five or ten minutes and compare them. If bright sunlight is not available, place the second tube in the light of a large electric bulb (200–300 watts) and compare the tubes after ten or fifteen minutes. If electric light is used, the tube must be placed very close to the bulb.

(B) *Baeyer's Test.* Add 1–2 cc. of the purified gasoline to a mixture of 3 cc. of dil. potassium permanganate solution (0.5 per cent) and 3 cc. of dil. sodium carbonate [2] solution (10 per cent), and shake well.

(C) Add 1–2 cc. of purified gasoline to about 3 cc. of concd. sulfuric acid.

(D) Add 1–2 cc. of purified gasoline to about 3 cc. of dil. sodium hydroxide solution (10 per cent).

(E) Add 1–2 cc. of purified gasoline to about 3 cc. of concd. nitric acid.

Ordinary Gasoline. Repeat the tests with ordinary gasoline.

Paraffin Oil. Repeat the tests with paraffin oil.

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[1] Ordinary gasoline may be purified to remove olefins by shaking once with half its volume of concd. sulfuric acid, then with small portions of fuming sulfuric acid (7 per cent or stronger) until the acid no longer becomes colored. It is then washed with water, dried over anhydrous calcium chloride, and decanted.

[2] Dil. sulfuric acid may be substituted for sodium carbonate. This substitution gives a better test reagent for certain purposes since manganese dioxide is not precipitated in the acid solution.

Unsat.

OBSERVATIONS ON HYDROCARBONS

Reagent	Purified Gasoline	Ordinary Gasoline	Paraffin Oil
Bromine water alone......			
Bromine water and light...			
Permanganate solution....			
Sodium hydroxide solution.			
Concd. sulfuric acid.......			
Concd. nitric acid.........			

Although the saturated hydrocarbons as a class are relatively inert, various reactions other than halogenation can be carried out under the activating influence of selected catalysts, high temperatures, etc. An illustrative example is the oxidation of commercial paraffin hydrocarbons by means of oxygen or air at 100–160°, with or without a catalyst, to give a mixture of monobasic carboxylic acids of varying molecular weights.

Ethane, propane, and butane, when subjected to the action of nitric acid and free oxygen in the vapor state at high temperature are converted to a mixture of nitroparaffins. Thus, propane gives a mixture of nitromethane, nitroethane, and the two nitropropanes; these aliphatic nitro compounds are now produced commercially by this process.

Saturated hydrocarbons containing a tertiary hydrogen ($R_3C—H$) are more reactive than other types. They can be sulfonated by fuming sulfuric acid to give sulfonic acids ($R_3C—SO_3H$) and can be added to an olefin in the presence of such catalysts as concd. sulfuric acid, aluminum chloride, or boron fluoride; thus, isobutane and ethylene give 2,2-dimethylbutane.

QUESTIONS

1. What substances are present in ordinary gasoline (which contains hydrocarbons made by the "cracking process") that are not present in purified gasoline? How may these substances be removed?

2. What is the chemical nature of paraffin oil? What is the origin of the name paraffin?

Experiment 10a

ETHYLENE (ETHENE)

(Short Experiment)

Support a 500-cc. round-bottom flask on an asbestos-centered wire-gauze, and provide it with a two-hole stopper which holds a glass delivery tube and a thermometer, the bulb of which reaches to within 1 cm. of the bottom of the flask. Bend the delivery tube to form two right angles and connect it by means of a one-hole stopper to a 200–300-cc. distilling flask, which serves as a safety-flask. Connect the side-tube of the safety-flask to a wash bottle half-filled with dil. sodium hydroxide solution (10 per cent). Prepare the wash bottle by providing a 250–300-cc. wide-mouth bottle with a two-hole stopper fitted with a glass inlet tube which extends to within 10–15 mm. of the bottom, and an outlet tube which extends only 5–10 mm. below the lower surface of the stopper. Arrange the outlet tube so as to bubble the gas through test solutions. The set-up is the same as the first part shown in Fig. 17.

Always polish the ends of all glass tubing in order to avoid injury to yourself and to avoid damaging the stoppers and rubber connections. It is advantageous to moisten a glass tube before attempting to insert it into a stopper or tight rubber connection.

In the 500-cc. flask, place 20 g. (25 cc.) of ordinary ethyl alcohol (95 per cent by volume), 110 g. (60 cc.) of concd. sulfuric acid and about 10 g. of amorphous silica.[1] Mix thoroughly by shaking and arrange the flask in its place, supported on an asbestos-centered wire-gauze. Heat the mixture rapidly to 150° and maintain a temperature of 155–160° by regulating the Bunsen burner. After the air has been displaced from the apparatus make the following tests on the gas.

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[1] The presence of amorphous silica (and many other inert substances) facilitates the decomposition of ethyl hydrogen sulfate (ethyl sulfuric acid) into ethylene and sulfuric acid. Among the substances which act in this way are: kieselguhr (infusorial earth), powdered pumice stone, and anhydrous aluminum sulfate (made by calcining ammonium alum).

(A) Bubble the ethylene through about 10 cc. of bromine water. Note the change which takes place and the odor of the product formed.

(B) *Baeyer's Test.* Bubble the ethylene through a mixture of about 5 cc. of dil. potassium permanganate solution (0.5 per cent) and 5 cc. of dil. sodium carbonate[1] solution (10 per cent).

➔ **Caution:** When the experiments have been completed, extinguish the flame and *immediately* disconnect the apparatus, in order to avoid any possibility of having the sodium hydroxide solution drawn back into the hot sulfuric acid mixture in the reaction flask.

Twenty years ago the dehydration of ethanol represented the commercial method for producing ethylene. Now, the conversion of ethylene to ethanol is an important industrial process. This is due to the fact that the commercial "cracking" of high molecular weight petroleum hydrocarbons gives enormous quantities of mixed olefins of low molecular weight. Individual olefins may be separated from the mixture by fractional distillation under pressure or may be removed selectively by their different rates of reactivity with reagents, especially sulfuric acid of definite concentration and temperature. Thus, a mixture of isobutylene, propylene, and ethylene can be treated successively with 65 per cent, 80 per cent, and 100 per cent sulfuric acid; at 35–40° only isobutylene is absorbed by the 65 per cent acid, propylene is absorbed by the 80 per cent acid, and ethylene only by the most concentrated acid.

Alcohols are formed upon dilution with water and distillation of the solution of the alkyl hydrogen sulfate formed by reaction of the olefin and sulfuric acid. Thus, ethylene gives ethanol; propylene, isopropanol; isobutylene, tertiary butanol, etc. These alcohols are now cheap commercial products.

Certain alcohols may also be made commercially by hydrolyzing the corresponding alkyl chlorides. Thus, by chlorination of *n*-pentane three isomeric pentyl chlorides are obtained; replacement of the chlorine by hydroxyl gives the three alcohols, pentanol-1, penantol-2, and pentanol-3, which may be separated by fractional distillation.

QUESTIONS

1. What is the purpose of the amorphous silica? the sodium hydroxide wash bottle?

2. What other methods may be used to dehydrate alcohols to obtain unsaturated hydrocarbons?

3. Compare ethane and ethylene in their behavior toward bromine.

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[1] Dil. sulfuric acid may be substituted for sodium carbonate. This substitution gives a better test reagent for certain purposes since manganese dioxide is not precipitated in the acid solution.

Experiment 10b

ETHYLENE AND ETHYLENE DIBROMIDE
(ETHENE AND 1,2-DIBROMOETHANE)

Arrange the apparatus[1] for this experiment in the following way: Support a 1-l. round-bottom flask (to serve as the generating flask) on an asbestos-centered wire-gauze, and provide it with a two-hole stopper which holds a glass delivery tube and a thermometer, the bulb of which reaches to within 1 cm. of the bottom of the flask. Bend the delivery tube to form two right angles and connect it by means of a one-hole stopper to a 200–300-cc. distilling flask, which serves as a safety-flask. Connect the side-tube of the safety-flask to a wash bottle half-filled with dil. sodium hydroxide solution (10 per cent). Prepare the wash bottle by providing a 150–250-cc. wide-mouth bottle with a two-hole stopper fitted with a glass inlet tube which extends to within 10–15 mm. of the bottom, and an

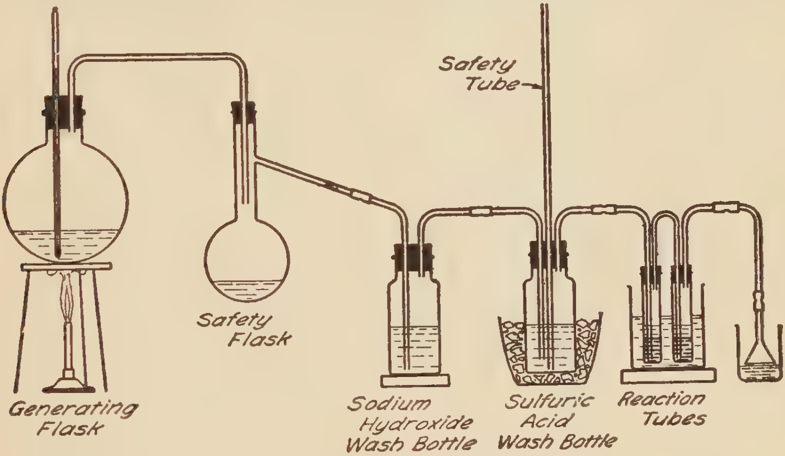

Fig. 17. — Apparatus for Ethylene Experiment.

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[1] If commercial cylinders of compressed ethylene (now used for anesthesia) are available, a cylinder of this gas may be used instead of the generating apparatus described here. Since the compressed ethylene for anesthesia is quite pure, it is unnecessary to use the sodium hydroxide and sulfuric acid wash bottles; however, it is advisable to pass the gas from the cylinder through a wash bottle containing pure water, in order to note and regulate the rate of passage of the gas.

outlet tube which extends only 5–10 mm. below the lower surface of the stopper. It is advisable to place an additional 50–60 cc. of strong sodium hydroxide solution (about 20 per cent) in the safety-flask, to aid in the removal of acidic impurities, and to avoid clogging the tube in the wash bottle through the precipitation of sodium salts. During the experiment it is well to cool the safety-flask from time to time by immersing it in a bath of cold water.

➔**Caution:** Always polish the ends of all glass tubing, in order to avoid injury to yourself and to avoid damaging the stoppers and rubber connections. It is advantageous to moisten a glass tube before attempting to insert it into a stopper or tight rubber connection.

Connect the outlet tube from the sodium hydroxide wash bottle to a wash bottle half-filled with cold concd. sulfuric acid. Provide this wash bottle with a three-hole stopper fitted with an inlet tube, an outlet tube, and a safety valve. The safety valve is a long glass tube (at least 75 cm. in length) which reaches to the bottom of the bottle. During the experiment, cool the sulfuric acid bottle in a mixture of ice and salt. Connect the outlet tube to a series of two reaction tubes for the bromine, which is divided into two equal portions in order to secure a rapid and more complete absorption of the ethylene. Prepare the reaction tubes by providing two specimen tubes (or test-tubes) with two-hole rubber stoppers which hold an inlet tube leading nearly to the bottom, and an outlet tube extending only 5–10 mm. below the lower surface of the stopper. Arrange the reaction tubes in series so that the purified ethylene from the sulfuric acid bottle passes through one tube and then through the other. During the experiment cool the bromine tubes in ice-water, *but not in a mixture of ice and salt.* (Why?) Toward the end of the experiment it is advisable to allow the temperature of the cooling bath to rise to about 10°, in order to avoid clogging the tube due to the solidification of the liquid. Connect the outlet from the second bromine tube to an ordinary 50–60 mm. funnel, which is inverted just above the surface of 100–150 cc. of water to which 10–20 cc. of a saturated sodium bisulfite solution has been added. Arrange all of the connections in the apparatus so that they are perfectly tight, and make the rubber connections as short as possible. Have the set-up approved by an instructor before placing the bromine in the tubes. Do not check

bromine from the stockroom until ready to use it, and do not allow it to stand in the desk from one laboratory period to another.

➔**Caution:** Handle bromine very carefully since the liquid produces painful burns, and the vapors are obnoxious. Treat burns immediately with a liberal quantity of glycerol.

When the apparatus is ready and has been approved, place 90 g. (110 cc.) of ordinary ethyl alcohol (95 per cent by volume) in the 1-l. generating flask and pour in slowly, with shaking, 184 g. (100 cc.) of concd. sulfuric acid. To this solution add 10–15 g. of amorphous silica,[1] and arrange the generating flask in its place. Disconnect the reaction tubes and place enough water in each to produce a layer 8–10 mm. in height. Divide 48 g. (15 cc.) of bromine into two approximately equal portions and place in the reaction tubes. Replace the tubes and see that all of the stoppers and rubber connections are tight.

Heat the generating flask rapidly to 150° and maintain a temperature of 155–165°, so that a steady, not too rapid, stream of ethylene is evolved. Continue the heating until the liquid in both of the reaction tubes is completely or almost completely decolorized. Disconnect the reaction tubes containing the ethylene dibromide, and make the following test before dismounting the ethylene generator.

Baeyer's Test. Bubble the ethylene through a mixture of about 5 cc. of dil. potassium permanganate solution (0.5 per cent) and 5 cc. of dil. sodium carbonate solution (10 per cent).[2]

When the experiment has been completed, extinguish the flame and immediately disconnect the safety-flask, to avoid having the sulfuric acid from the wash bottle sucked back into the sodium hydroxide solution as cooling takes place. During the experiment the mixture in the flask should not carbonize too much. If this does occur (from overheating), it will probably be necessary to empty the flask and start again with a fresh mixture of alcohol and sulfuric acid, using half the original quantities of material.

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[1] The presence of amorphous silica (and many other inert substances) facilitates the decomposition of ethyl hydrogen sulfate (ethyl sulfuric acid) into ethylene and sulfuric acid. Among the substances which act in this way are: kieselguhr (infusorial earth), powdered pumice stone, and anhydrous aluminum sulfate (made by calcining ammonium alum).

[2] Dil. sulfuric acid may be substituted for sodium carbonate. This substitution gives a better reagent for certain purposes since manganese dioxide is not precipitated in the acid solution.

Unite the contents of both reaction tubes, transfer to a small cylindrical separatory funnel, and wash with about 25 cc. of water to which a few drops of a saturated solution of sodium bisulfite have been added. If the reaction product was not already colorless, it should be so at this point. If not, add a few drops more of the saturated sodium bisulfite solution and shake well. Separate the product from the aqueous solution, wash with 25–30 cc. of a saturated sodium bicarbonate solution, and finally with 25–30 cc. of pure water. After the last washing separate very carefully from the water and drain the product into a small dry Erlenmeyer flask. Add 5–6 g. of anhydrous calcium chloride and shake the mixture gently for a few moments. The liquid should be allowed to stand with calcium chloride for at least thirty minutes to obtain good drying. It may stand longer without harm.

Through a funnel containing a small plug of cotton, decant the dried liquid into a small dry distilling flask, add two small chips of clay plate, and distil. Collect the product boiling at 127–132° in a weighed bottle. If a considerable amount of low boiling material is obtained, dry this again with 3–4 g. of anhydrous calcium chloride and redistil. The yield is 35–40 g.

For a discussion of olefins see page 109.

QUESTIONS

1. What is the purpose of the amorphous silica? the sodium hydroxide wash bottle? the sulfuric acid wash bottle? Why is the latter kept cold? Why is the product washed with sodium bisulfite solution?
2. What other methods may be used to convert alcohols to unsaturated hydrocarbons?
3. Compare ethane and ethylene in their behavior toward bromine.
4. Write equations for one other general method of preparing hydrocarbons of the ethylene series.
5. Show how the general methods for preparing olefins may be applied to the preparation of butene-1.
6. In what important commercial process is propene obtained as a by-product? What use is made of this propene?

Experiment 11a

AMYLENE (PENTENE-2)

Place 35 cc. of water in a 200-cc. round-bottom flask and add cautiously, with shaking, 65 g. (35 cc.) of concd. sulfuric acid. Cool the solution to room temperature or slightly below, and add slowly 30 g. (36 cc.) of pentanol-2. Connect the flask with a long efficient condenser (60–70 cm. in length) by means of a bent glass tube, and provide the lower end of the condenser with an adapter which passes well into a 100–150-cc. Erlenmeyer flask surrounded by an ice-bath.

Heat the flask on a steam-bath as long as any liquid distils (about two hours is required). Treat the distillate with about 10 cc. of dil. sodium hydroxide solution (10 per cent), shake thoroughly, and transfer to a separatory funnel. Separate the lower aqueous layer and pour the hydrocarbon layer through the mouth of the funnel (Why?) into a small dry flask or bottle. Add about 2 g. of anhydrous calcium chloride and allow to dry for twenty to thirty minutes, with occasional shaking.

Through a funnel containing a small plug of cotton, decant the dried product into a distilling flask of the proper size, add a few small chips of clay plate, and distil from a water-bath. Collect in a weighed bottle the portion boiling at 35–41°. The yield is 12–15 g.

➔**Caution:** Amylene [1] is extremely volatile and is inflammable. Take care to avoid fire hazard and to minimize loss through evaporation.

Tests for Unsaturation

(A) Add 1–2 cc. of amylene to 3 cc. of bromine water and shake.

(B) *Baeyer's Test.* Add 1–2 cc. of amylene to a mixture of 3 cc. of dil. potassium permanganate solution (0.5 per cent) and 3 cc. of dil. sodium carbonate [2] solution (10 per cent) and shake.

(C) Add 1–2 cc. of amylene to 3 cc. of concd. sulfuric acid.

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[1] Amylene is a name applied to any of the isomeric pentenes or mixtures of pentenes, which are usually obtained by dehydration of the amyl alcohols ($C_5H_{11}OH$). Olefin is a general name applied to any hydrocarbon of the ethylene series.

[2] Dil. sulfuric acid may be substituted for sodium carbonate. This substitution gives a better test reagent for certain purposes since manganese dioxide is not precipitated in the acid solution.

Experiment 11b

CYCLOHEXENE

Place 20 g. (21 cc.) of cyclohexanol (a technical grade is satisfactory) and 2 cc. of concd. sulfuric acid in a 200-cc. round-bottom flask, and mix thoroughly. Provide the flask with a short fractionating column and a long condenser (see Fig. 11, page 47) and fit the lower end of the condenser with an adapter which passes well into a 100–150-cc. receiver surrounded by an ice-bath.

Add two chips of clay plate and heat the flask gently over a wire-gauze with a small flame, so that the cyclohexene and water distil through the column. The temperature at the top of the column should not be allowed to rise above 100°. Continue the distillation until only a small residue remains:

Saturate the distillate with clean salt (sodium chloride), and add 1–2 cc. of sodium carbonate solution to neutralize traces of acid. Allow the layers to separate and draw off the lower, aqueous layer. Pour the hydrocarbon layer through the mouth of the funnel (Why?) into a small dry flask or bottle, add 3–4 g. of anhydrous calcium chloride and allow to stand for twenty minutes, with occasional shaking. Through a funnel containing a small plug of cotton, decant the dried product into a small, simple distilling flask, add a few small chips of clay plate, and distil. Collect the portion boiling at 80–85° in a weighed bottle. If an appreciable low-boiling fraction is obtained, dry this again and redistil. The yield is 10–12 g.

Carry out the *Tests for Unsaturation* (page 119), using cyclohexene instead of amylene.

QUESTIONS

1. Write structural formulas for all of the isomeric pentenes (C_5H_{10}).
2. Which one of the isomeric pentenes is likely to be present in addition to pentene-2 in the amylene prepared by dehydration of pentanol-2? Explain.
3. What product would be formed from cyclohexene by addition of hypochlorous acid? by addition of ozone, and subsequent hydrolysis of the ozonide?
4. What is the meaning and derivation of the name olefin?

Experiment 12

ACETYLENE (ETHYNE)

In a 200-cc. distilling flask, the neck of which is closed by a cork fitted with a separatory funnel, place 8–10 g. of technical calcium carbide. Connect the side-tube of the flask with a glass delivery tube bent so as to be able to pass the gas into test solutions. From the separatory funnel, allow water to fall drop by drop upon the calcium carbide. As soon as the air has been displaced from the flask make the following tests on the gas.

(A) Bubble the gas through about 10 cc. of dil. bromine water. Note the changes which take place and the odor of the product formed.

(B) *Baeyer's Test.* Bubble the gas through a mixture of about 5 cc. of dil. potassium permanganate solution (0.5 per cent) and 5 cc. of dil. sodium carbonate[1] solution (10 per cent).

(C) Bubble the gas through about 5 cc. of a 5 per cent solution of silver nitrate to which 5 drops of concd. aqueous ammonia have been added. Pour off the liquid and to the precipitate, silver acetylide, add about 5 cc. of dil. nitric acid (1 vol. of concd. nitric acid to 1 vol. of water), and warm gently.

➔**Caution:** Silver and copper acetylides are dangerously explosive when in a dry condition. Do not leave any of the precipitates obtained in (C) and (D) in your desk or in the waste jars. Destroy the acetylides by boiling with dil. nitric acid before leaving the laboratory.

(D) Bubble the gas through about 10 cc. of an ammoniacal solution of cuprous chloride (prepared as described below). Filter the precipitate with suction on a small Büchner funnel and transfer to a test-tube. Treat the precipitate, copper acetylide, with about 5 cc. of dil. nitric acid (1 vol. of concd. nitric acid to 1 vol. of water), and warm gently.

Preparation of Ammoniacal Cuprous Chloride Solution. Dissolve 3.5 g. of hydrated copper sulfate ($CuSO_4$, $5H_2O$) and 1 g. of sodium

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[1] Dil. sulfuric acid may be substituted for sodium carbonate. This substitution gives a better test reagent for certain purposes since manganese dioxide is not precipitated in the acid solution.

chloride in 12 cc. of hot water and add with shaking a solution of 1 g. of sodium bisulfite in 10 cc. of 5 per cent sodium hydroxide solution. Cool to room temperature and wash the precipitated cuprous chloride by decantation. Dissolve the precipitate in 10–15 cc. of a mixture of equal volumes of concd. aqueous ammonia and water.

(E) Observe the color, solubility, inflammability, and odor of the gas. Pure acetylene is almost odorless; the characteristic odor of ordinary acetylene may be due to small amounts of the hydrides of sulfur, arsenic, and phosphorus. Explain the source of these impurities.

Acetylene, in recent years, has become a very important raw material in organic chemistry. It adds water in presence of mercury salts to give acetaldehyde, which in turn may be oxidized to acetic acid. By addition of acetic acid in the presence of mercury salts, acetylene gives ethylidene diacetate, which may be pyrolized either to vinyl acetate and acetic acid, or to acetaldehyde and acetic anhydride.

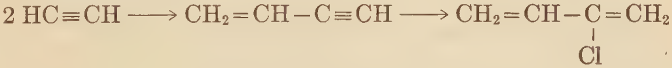
$$HC\equiv CH + H_2O \longrightarrow CH_3CHO \longrightarrow CH_3COOH$$

$$HC\equiv CH + 2\,CH_3COOH \longrightarrow CH_3CH(OCOCH_3)_2 \longrightarrow$$

$$CH_3CHO + (CH_3CO)_2O \quad \textit{or} \quad CH_2{=}CHOCOCH_3 + CH_3COOH$$

Acetylene adds one mole of hydrogen chloride to give vinyl chloride, and adds two moles of chlorine to give the important solvent acetylene tetrachloride. Both vinyl chloride and vinyl acetate polymerize to yield substances used in the preparation of artificial resins.

In presence of copper salts, two molecules of acetylene react to form vinyl acetylene, which adds hydrogen chloride to yield 2-chloro-1,3-butadiene (chloroprene). Chloroprene on polymerization gives the synthetic rubber, neoprene.



$$2\,HC\equiv CH \longrightarrow CH_2{=}CH{-}C\equiv CH \longrightarrow CH_2{=}CH{-}\underset{\substack{|\\ Cl}}{C}{=}CH_2$$

QUESTIONS

1. What are the important uses of acetylene?
2. How is calcium carbide prepared?
3. How may acetaldehyde be prepared from acetylene?
4. Write equations illustrating the preparation of methylacetylene (propyne).

Experiment 13

ETHYL ALCOHOL (ETHANOL)

By Fermentation of Sugar

Place 80 g. of sucrose (ordinary granulated sugar) in a 1-l. Florence flask, add about 700 cc. of water, 70 cc. of a solution of Pasteur's salts,[1] and one-half cake of compressed yeast rubbed to a thin paste with 30–40 cc. of water. Shake vigorously and close the flask with a rubber stopper holding a delivery tube arranged so that any gas which is evolved must bubble through about 10 cc. of a clear solution of barium hydroxide in a test-tube. Protect the barium hydroxide from carbon dioxide of the air by a 4–5 mm. layer of paraffin oil or kerosene. Allow the mixture to stand at a temperature of about 25° until fermentation is complete, as indicated by the cessation of gas evolution (usually about a week is required).

Without stirring up the yeast any more than is necessary, decant the liquid through a small plug of cotton or glass wool into a 1-l. round-bottom flask. Connect the flask by means of a bent glass tube (about 8 mm. in diam.) with a condenser set downward for distillation and distil off 200–250 cc. of liquid. Discard the residue remaining in the flask. Transfer the distillate to a 500-cc. round-bottom flask, arrange a fractionating column and distil slowly (*cf.* Exp. 4). Collect the following fractions: A, 78–82°; B, 82–88°; C, 88–95°. Discard the residue and redistil the fractions A, B, and C to separate as large a quantity of 95 per cent alcohol as possible. Salt out the alcohol from fraction B by adding solid anhydrous potassium carbonate until the liquid is saturated. Shake well, decant the liquid from any solid material into a small dry separatory funnel, and allow the layers to separate. Draw off the lower aqueous layer and pour the upper layer into fraction A. Redistil the fraction A from a small distilling flask and collect the fraction boiling at 78–82° in a clean weighed receiver.

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[1] Pasteur's salts solution consists of: potassium phosphate 2.0 g., calcium phosphate 0.20 g., magnesium sulfate 0.20 g., ammonium tartrate 10.0 g., in 860 g. of water.

Carry out the *Iodoform Test* and *Esterification Test* (see Exp. 14) with small portions of the product.

The fermentation processes involved in bread making, wine making, and brewing are among the oldest chemical arts. For many years it was believed that the transformation of sugar by yeasts into alcohol and carbon dioxide was inseparably connected with the life process of the yeast cell. This view was abandoned, however, when Buchner demonstrated that yeast juice will bring about alcoholic fermentation in the absence of any yeast cells. The fermenting activity of yeast is due to a remarkably active catalyst of biochemical origin, the enzyme zymase. It is now recognized that most of the chemical transformations that go on in living cells of plants and animals are brought about by enzymes.

Enzymes show an extraordinary specificity—a given enzyme can act only on a specific compound, or closely related group of compounds. Thus, zymase acts only on a few specific sugars and not on all carbohydrates; the digestive enzymes of the alimentary tract are equally specific in their activity.

In the alcoholic fermentation of disaccharides such as maltose or sucrose ($C_{12}H_{22}O_{11}$) the first step is an hydrolysis to hexoses ($C_6H_{12}O_6$) by the enzyme maltase or invertase, which is present in yeast in addition to zymase. The hexoses are then converted by zymase into alcohol and carbon dioxide. Pasteur observed that growth and fermentation were promoted by the addition of small amounts of mineral salts to the nutrient medium. Later it was found that, prior to fermentation, the hexose sugars combine with phosphoric acid and the resulting hexose-phosphoric acid combination is then split up into carbon dioxide and alcohol.

Yeasts, molds, and bacteria are used commercially for the large scale production of various organic compounds. An important example, in addition to ethyl alcohol, is the anerobic fermentation of starch by certain bacteria to yield *n*-butyl alcohol, acetone, and hydrogen.

QUESTIONS

1. Does the yeast increase in quantity during the fermentation?
2. What is fusel oil? Write the structural formulas of the most important constituents of fusel oil.
3. Mention several methods which are used to determine the amount of alcohol in water-alcohol mixtures.
4. What is *absolute* alcohol? How is it obtained?
5. What is proof spirit? What is meant by 180-proof?

Experiment 14

REACTIONS OF ALCOHOLS

(A) **Iodoform Test.** In a test-tube place 2 cc. of the liquid to be tested, add 2–3 cc. of water, and 8–10 cc. of a 10 per cent solution of iodine in potassium iodide (prepared by dissolving 10 g. of iodine crystals in a solution of 20 g. of potassium iodide in 80 cc. of water). Then add sodium hydroxide solution (10–20 per cent), drop by drop, until the brown color of the iodine is discharged and the liquid retains only a yellow color. With some compounds a precipitate of iodoform forms immediately in the cold. Warm the tube to 60° in a water-bath for two minutes, and cool. If a precipitate is formed, note its appearance and odor. It is wise to confirm the identity of the iodoform by filtering, drying the crystals, and taking the melting-point.

Carry out the iodoform test with ethyl alcohol, *n*-propyl alcohol, and *sec*-butyl alcohol.

The formation of iodoform is an example of the haloform reaction, which is typical of methyl ketones ($CH_3—CO—R$) and of secondary alcohols of the type $CH_3—CHOH—R$. Only one aldehyde ($CH_3—CH{=}O$) and only one primary alcohol ($CH_3—CH_2OH$) give a positive iodoform test. (Explain!) An excellent discussion and review of the haloform reaction has been published recently.[1]

(B) **Esterification Test.** Mix 3 cc. of the liquid to be tested with 2 cc. of glacial acetic acid, and add cautiously 2 cc. of concd. sulfuric acid. Mix thoroughly and warm gently; add 5 cc. of water and note the odor of the vapor, with caution.

Carry out this test with ethyl alcohol, *sec*-butyl alcohol, and *tert*-butyl alcohol. Primary alcohols, and most secondary alcohols, of low molecular weight are converted into volatile esters (acetates) having a characteristic odor different from that of the alcohol itself. Tertiary alcohols are not esterified under these conditions.

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[1] Fuson and Bull, *Chemical Reviews*, **15**, 275 (1934).

(C) **Action of Sodium.** Place 5 cc. of *absolute* ethyl (or methyl) alcohol in a test-tube, drop in a very small piece of bright metallic sodium (handle carefully),[1] and observe.

This reaction is of little or no practical value as a simple test reaction, since it could be applied only to pure, anhydrous liquids. Traces of water or organic acids, present as impurities in an inert liquid, would evolve hydrogen and give a misleading result. Certain ketones and esters also evolve hydrogen when treated with metallic sodium.

(D) **Oxidation Test.** To 5 cc. of a 1 per cent solution of sodium dichromate, add one drop of concd. sulfuric acid and mix thoroughly by shaking. Add 2 drops of the liquid to be tested, and warm gently. Note the odor, and observe any change in color of the solution.

Carry out this test with ethyl alcohol, *sec*-butyl alcohol, and *tert*-butyl alcohol.

(E) **Differentiation of Primary, Secondary, and Tertiary Alcohols.** *Lucas' Test.* The reagent used is concd. hydrochloric acid containing one mole of fused zinc chloride to one mole of the acid.[2] The differentiation is based upon the rate of formation of the alkyl chlorides from the alcohols with the test reagent, and with concd. hydrochloric acid.

To 1 cc. of the alcohol add quickly 6 cc. of the hydrochloric acid-zinc chloride reagent at 26–27°. Close the tube with a cork and shake; then allow the mixture to stand. Observe carefully for the first five minutes, and again after one hour. Note the time required for reaction to take place, as indicated by the cloudy appearance of the solution, and whether or not two immiscible layers finally separate. If the result is positive, carry out a second test using concd. hydrochloric acid alone, instead of the test reagent, and observe.

Perform the Lucas test with *n*-propyl alcohol, *iso*-amyl alcohol, *tert*-butyl alcohol, and *sec*-butyl alcohol. Other alcohols that are available may also be tested (*e.g.*, an "unknown" alcohol furnished by the instructor).

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[1] Metallic sodium must be handled with tongs or pincers—not with the fingers. Do not throw small residual scraps of sodium into water or into a waste jar; place them in a bottle provided for this purpose.

[2] Lucas' reagent is prepared by dissolving 34 g. of anhydrous (fused) zinc chloride in 27 g. (23 cc.) of concd. hydrochloric acid, with stirring and external cooling to avoid loss of hydrogen chloride. The resulting solution has a volume of about 35 cc. and is sufficient for five individual tests.

The lower alcohols through C_5H_{11}—OH are soluble in Lucas' reagent. Tertiary alcohols react at once to give the alkyl chloride, as indicated by the development of a cloudy appearance; the chloride is sparingly soluble in the reagent and soon forms a distinct layer. Secondary alcohols react within five minutes to give a cloudy appearance, and a distinct layer appears later. Saturated primary alcohols do not react at ordinary temperatures and the solution remains clear. If small amounts of secondary or tertiary alcohols are present as impurities in a primary alcohol, some cloudiness may be observed, but a distinct layer of alkyl halide will not separate on standing. Separation into two distinct layers on standing will occur only if the test liquid contains an appreciable quantity of secondary or tertiary alcohol.

The differentiation of secondary and tertiary alcohols is confirmed by a supplementary test with concd. hydrochloric acid alone. A tertiary alcohol reacts rapidly to form the chloride, which forms a separate layer in a few minutes. The solution of a secondary (or primary) alcohol remains clear, since neither will form an alkyl chloride under the conditions of the supplementary test.

iso-Propyl alcohol does not always show the characteristic behavior of a secondary alcohol, due presumably to the circumstance that *iso*-propyl chloride is very volatile (b.p. 36°) and may escape from the solution. Certain very reactive primary alcohols (CH_2=CH—CH_2OH, C_6H_5—CH_2OH, etc.), and higher molecular weight compounds, behave in a non-typical manner.[1]

QUESTIONS

1. Explain why methyl alcohol does not give the iodoform test.

2. Write the structural formulas for the following alcohols, and indicate whether or not the alcohol would give a positive iodoform test: *iso*-propyl alcohol (propanol-2); *iso*-butyl alcohol (methyl-2-butanol-1); methyl *iso*-butyl carbinol (methyl-4-pentanol-2).

3. Write the structural formulas and names for two of the isomeric amyl alcohols (C_5H_{11}—OH) which would give a positive reaction in the Lucas test but a negative iodoform test.

[1] Lucas. *J. Am. Chem. Soc.*, **52**, 803 (1930).

Experiment 15a

n-BUTYL BROMIDE (1-BROMOBUTANE)

Hydrobromic Acid—Sulfuric Acid Method

Preparation of Hydrobromic Acid—Sulfuric Acid Solution.[1] In a 500-cc. round-bottom flask, weigh out 65 g. of chopped ice and add 56 g. (17 cc.) of bromine. Place the flask in an ice-bath and bubble sulfur dioxide (from a commercial cylinder) into the mixture until the bromine color disappears. Agitate the mixture occasionally, especially at the start, until the bromine has passed into solution. At the end of the reaction a straw-colored liquid is obtained, which contains hydrobromic and sulfuric acids, along with some dissolved sulfur dioxide. Use this solution directly for the preparation of *n*-butyl bromide.

➔**Caution:** Handle bromine very carefully—the liquid produces painful burns and the vapors are obnoxious. Treat burns immediately with a liberal quantity of glycerol.

Fit the 500-cc. flask containing the hydrobromic acid—sulfuric acid solution with a water-cooled reflux condenser. In the top of the condenser place a cork bearing a delivery tube bent twice at right angles to form a U. Connect this by means of a short rubber tube to a 50–60 mm. funnel inverted over 250–300 cc. of water in a large beaker.[2] This arrangement is made to absorb hydrogen bromide and sulfur dioxide which may be evolved upon heating and which must not be allowed to escape into the room.

Remove the reaction flask and add, with shaking, 37 g. (46 cc.) of *n*-butyl alcohol (butanol-1) and then an additional 25 g. (13–14 cc.) of concd. sulfuric acid. Put in a few chips of clay plate to prevent bumping, quickly adjust the reflux condenser, and boil gently on a wire-gauze for two hours. Cool the contents of the flask

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[1] The hydrobromic acid—sulfuric acid solution can also be prepared by adding 35 g. (19 cc.) of concd. sulfuric acid to 120 g. (80 cc.) of 48 per cent hydrobromic acid.

[2] Another suitable arrangement may be made by connecting the rubber tube to a glass tube supported *above* a surface of water in a suction filtering flask.

slightly, remove the condenser, set it downward for distillation, and connect it with the flask by means of a bent glass tube (about 8 mm. in diam.). Distil the reaction mixture until no more butyl bromide passes over (about one-half hour).

Transfer the distillate to a separatory funnel and add about 50 cc. of water. If the product is colored, due to the presence of free bromine, add 3–5 cc. of a saturated sodium bisulfite solution. Shake well and decant the *n*-butyl bromide (which layer?). Wash again in a dry separatory funnel with about 25 cc. of concd. sulfuric acid which has previously been cooled in an ice-bath. Separate from the sulfuric acid (which layer?) and wash the *n*-butyl bromide with water, then with 25–30 cc. of a saturated sodium bicarbonate solution, and finally with water. After a final washing, separate very carefully from the water, collect the product in a small dry flask, and dry with 5–10 g. of anhydrous calcium chloride. In order to obtain satisfactory drying, the liquid should be allowed to remain in contact with anhydrous calcium chloride for at least thirty minutes, with occasional shaking.

Through a funnel containing a small plug of cotton, decant the dried product into a distilling flask of the proper size, add a few small chips of clay plate, and distil on an asbestos-centered wire-gauze. Collect in a weighed bottle the portion boiling at 99–103°. If a considerable amount of low boiling material is obtained, dry this again with 3–4 g. of anhydrous calcium chloride and redistil. The yield is 55–60 g.

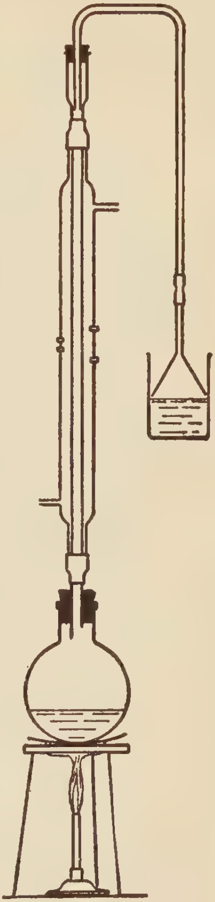

FIG. 18. — Apparatus for *n*-Butyl Bromide Experiment.

For questions see page 143.

Experiment 15b

n-BUTYL BROMIDE (I-BROMOBUTANE)

Sodium Bromide—Sulfuric Acid Method

In a 500-cc. round-bottom flask, place 60–70 cc. of water and then add 87 g. of finely pulverized sodium bromide ($NaBr, 2H_2O$). Shake the mixture thoroughly to avoid the formation of lumps and add 37 g. (46 cc.) on *n*-butyl alcohol (butanol-1). Attach a reflux condenser to the flask and add 129 g. (70 cc.) of concd. sulfuric acid (in portions of about 10 cc.) through the top of the condenser while the flask is being shaken (some hydrogen bromide is usually evolved during this addition). Good mixing is essential.

After all of the sulfuric acid has been added, place in the top of the condenser a cork bearing a delivery tube bent twice at right angles to form a U. Connect this by means of a short rubber tube to a 50–60 mm. funnel inverted over 250–300 cc. of water in a large beaker (see Fig. 18, Exp. 15a). Add a few chips of clay plate to prevent bumping and reflux the mixture on an asbestos-centered wire-gauze for two hours. Cool the flask slightly, remove the condenser, set it downward for distillation, and connect it with the flask by means of a bent glass tube (about 8 mm. in diam.). Distil the reaction mixture until all the butyl bromide has passed over (about one-half hour).

Transfer the distillate to a separatory funnel and add about 50 cc. of water. If the product is colored, due to the presence of free bromine, add 3–5 cc. of a saturated sodium bisulfite solution. Shake well and decant the *n*-butyl bromide (which layer?). Wash again in a dry separatory funnel with about 25 cc. of concd. sulfuric acid which has previously been cooled in an ice-bath. Separate from the sulfuric acid (which layer?) and wash the *n*-butyl bromide with water, then with 25–30 cc. of a saturated sodium bicarbonate solution, and finally with water. After the final washing, separate very carefully from the water, collect the product in a small dry flask, and dry with 5–10 g. of anhydrous calcium chloride. To in-

sure satisfactory drying allow the liquid to remain in contact with anhydrous calcium chloride for at least thirty minutes, with occasional shaking.

Through a funnel containing a small plug of cotton, decant the dried product into a distilling flask of the proper size, add a few small chips of clay plate and distil. Collect in a weighed bottle the portion boiling at 99–103°. If a considerable amount of low boiling material is obtained, dry this again with 3–4 g. of anhydrous calcium chloride and redistil. The yield is 45–50 g.

QUESTIONS

1. Why is the crude *n*-butyl bromide washed with concd. sulfuric acid?

2. Write equations illustrating: another method of preparing *n*-butyl bromide from *n*-butyl alcohol; the preparation of *n*-butyl chloride from *n*-butyl alcohol; the preparation of *n*-butyl iodide from *n*-butyl alcohol.

3. What is the order of the reactivity of the halogen atoms in the three butyl halides mentioned in the preceding question?

4. Write equations indicating how each of the following compounds may be obtained from *n*-butyl bromide: *n*-butane; *n*-octane; butene-1; butanol-1.

5. What is meant by the term, Grignard reagent? Illustrate by writing the equation for the preparation of a Grignard reagent from *n*-butyl bromide.

6. Which of the halogen acids reacts most readily with an alcohol to form the alkyl halide? Which reacts least readily?

Experiment 15c

tert-BUTYL CHLORIDE

In a 250-cc. separatory funnel, place 148 g. (125 cc.) of concd. hydrochloric acid (sp. g. 1.18) which has been cooled to 5°. Add 28 g. (35 cc.) of technical *tert*-butyl alcohol (equivalent to about 25 g. of anhydrous alcohol) and shake the mixture occasionally during twenty minutes. From time to time relieve any internal pressure by inverting the funnel and slowly opening the stopcock. Allow the mixture to stand undisturbed until the layers have separated sharply, then draw off and discard the spent hydrochloric acid (which layer?). Wash the product with 10–15 cc. of water, then with 5 per cent sodium bicarbonate solution, and again with water. Transfer the chloride to a small dry flask and dry with 5–6 g. of anhydrous calcium chloride. Decant the dried liquid through a funnel containing a small plug of cotton into a dry distilling flask, add a few small chips of clay plate, and distil. Collect the fraction boiling at 49–51° in a weighed bottle. The yield is 20–24 g. If a considerable low-boiling fraction is obtained, dry this again with calcium chloride, and redistil.

QUESTIONS

1. Could *n*- and *sec*-butyl alcohols be converted to the chlorides merely by shaking with concd. hydrochloric acid? (*cf.* Lucas' Test, Exp. 14, page 133).
2. Which of the halogen acids reacts most readily with an alcohol to form the alkyl halide? Which reacts least readily?
3. Write an equation showing the preparation of a Grignard reagent from *tert*-butyl chloride. What would be formed if this Grignard reagent were treated with water?
4. What is formed by warming *tert*-butyl chloride with sodium hydroxide solution?

***sec*-Butyl Chloride (Alternative Experiment).** In a 200-cc. round-bottom flask, place 90 g. of anhydrous zinc chloride and 63 g. (55 cc.) of concd. hydrochloric acid which has been cooled to 5°. Shake the mixture and keep it cool until the zinc chloride has dissolved, then add 25 g. (31 cc.) of *sec*-butyl alcohol. Attach a reflux condenser, add a few chips of clay plate, and boil the mixture briskly on a wire-gauze for two hours. Cool the reaction mixture and transfer to a separatory funnel. Draw off and discard the lower, aqueous layer.

Transfer the crude butyl chloride to a 200-cc. round-bottom flask and add an equal volume of concd. sulfuric acid. Attach a reflux condenser, heat until the butyl chloride boils gently, and continue the boiling for fifteen minutes. This treatment eliminates impurities which are not removed by ordinary distillation. Cool the flask slightly, remove the condenser, set it downward for distillation, and connect it with the flask by a wide, bent glass tube. Distil off the *sec*-butyl chloride (avoiding excessive heating of the residual sulfuric acid) and transfer the distillate to a separatory funnel. Wash the product with water, decant into a small dry flask, and dry with 5–6 g. of anhydrous calcium chloride. Decant the dried liquid through a funnel containing a small plug of cotton into a small dry distilling flask, add a few small chips of clay plate, and redistil. Collect the fraction boiling at 67–69° in a weighed receiver. The yield is 18–24 g. If a considerable low-boiling fraction is obtained, dry this again with calcium chloride, and redistil.

QUESTIONS

1. Could *n*- and *sec*-butyl alcohols be converted to the chlorides merely by shaking with concd. hydrochloric acid? (*cf*. Lucas' Test, Exp. 14, page 133).
2. Which of the halogen acids reacts most readily with an alcohol to form the alkyl halide? Which reacts least readily?
3. Write an equation showing the preparation of a Grignard reagent from *tert*-butyl chloride. What would be formed if this Grignard reagent were treated with water?
4. What is formed by warming *tert*-butyl chloride with sodium hydroxide solution?

Experiment 15d

ETHYL IODIDE (IODOETHANE)

In a 200-cc. round-bottom flask, place 2.5 g. of red phosphorus and 24 g. (30 cc.) of ordinary ethyl alcohol (95 per cent by volume), and add gradually, during the course of fifteen minutes, 25 g. of pulverized iodine. During the addition of the iodine, shake the flask frequently and keep the mixture cool by dipping in cold water. Connect the flask with a water-cooled reflux condenser (at least 50–60 cm. in length) and allow the reaction mixture to stand at least four hours. There is no objection to the reaction mixture standing longer, if a cork is placed loosely in the top of the condenser to prevent evaporation of the volatile ethyl iodide. If this is done, the removal of the stopper before proceeding further must not be forgotten. In order to complete the reaction, heat the mixture very gently for two hours on a steam-bath. During this heating it is necessary to keep the condenser well cooled and to avoid violent boiling of the mixture in order to minimize the loss of the volatile ethyl iodide.

Cool the contents of the flask thoroughly, remove the condenser, set it downward for distillation, and connect it with the flask by means of a bent glass tube (about 8 mm. in diam.). Provide the end of the condenser with an adapter which dips just below the surface of about 200 cc. of ice and water, and distil the ethyl iodide, by heating the flask in a steam-bath or a rapidly boiling water-bath. To drive over the last traces of ethyl iodide, which distil with difficulty, dry the outside of the flask and heat gently for a short time with a small luminous flame kept in constant motion.

Transfer the distillate to a separatory funnel and decant the ethyl iodide, which is usually colored brown by the presence of free iodine. Wash the ethyl iodide with about 50 cc. of water and, to remove the iodine, wash with water to which a few drops of dil. sodium hydroxide solution (10 per cent) have been added. Separate the heavy, almost colorless oil, and allow to dry for about two hours with 2–3 g. of anhydrous calcium chloride, in a corked flask or bottle.

Through a funnel containing a small plug of cotton or glass wool, decant the dried product into a small dry distilling flask. Distil slowly and carefully from a water-bath, and collect in a dry weighed bottle the portion which boils at 70–75°. The yield is 15–20 g. If the product is pure and dry, it will be colorless and perfectly clear. If the product is turbid, this indicates the presence of moisture. In this case, dry again with 1–2 g. of anhydrous calcium chloride and redistil. Ethyl iodide usually becomes violet or brown colored on standing. A globule of mercury placed in the bottle will keep the product colorless (Why?).

QUESTIONS

1. Can ethyl iodide be prepared by the action of iodine on ethane?
2. How could ethyl iodide be prepared from ethyl bromide?
3. How could ethyl bromide be prepared from ethyl iodide?
4. Of the three ethyl halides, ethyl iodide, ethyl bromide, and ethyl chloride: which is the most reactive? which is the least reactive?
5. Write equations indicating how each of the following compounds may be obtained from ethyl iodide: ethane; *n*-butane; ethylene; ethyl alcohol.
6. What is meant by the term, Grignard reagent? Illustrate by writing an equation for the preparation of a Grignard reagent from ethyl iodide.

C_2H_5C = [illegible]

Experiment 16

DIETHYL ETHER

Support a 500-cc. round-bottom flask on an asbestos-centered wire-gauze and provide it with a three-hole stopper holding a bent delivery tube (about 8 mm. in diam.), a cylindrical separatory funnel, and a thermometer, the bulb of which reaches to within 1 cm. of the bottom of the flask. The lower end of the stem of the separatory funnel should extend about 8–10 mm. below the surface of the alcohol-sulfuric acid mixture. The stem may be lengthened if necessary by attaching a short glass tube by means of a short rubber tube. By means of a one-hole stopper or cork, connect the delivery tube to a long water-cooled condenser (60–70 cm. in length) set downward for distillation, and fit the lower end of the condenser with a 200–250-cc. distilling flask to serve as a receiver. Cool the latter in a mixture of ice and salt, and provide the side-tube with a rubber tube which conducts any uncondensed vapors to the floor.

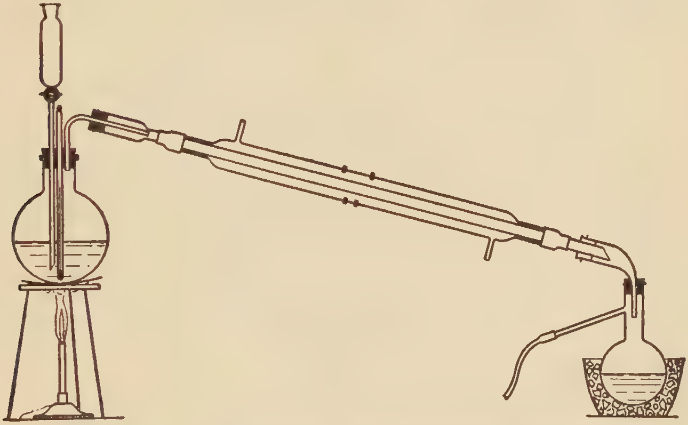

FIG. 19.—Apparatus for Diethyl Ether Experiment.

In the round-bottom flask place 40 g. (50 cc.) of ordinary ethyl alcohol (95 per cent by volume) and add slowly with constant shaking 92 g. (50 cc.) of concd. sulfuric acid. Heat the flask on an

asbestos-centered wire-gauze until the temperature reaches 140° and add slowly 80 g. (100 cc.) of alcohol through the separatory funnel as fast as the ether distils out. Regulate the flame so that the temperature does not fall below 140° nor rise above 150°. Continue the heating for five or ten minutes after all the alcohol has been added.

Transfer the distillate, which contains ether, alcohol, water, and sulfurous acid, to a separatory funnel and wash with 30–40 cc. of dil. sodium hydroxide solution (10 per cent). Draw off the sodium hydroxide solution and wash the product with an equal volume of a strong calcium chloride solution (40–50 per cent). Separate the calcium chloride solution from the ether, pour the ether through the mouth of the separatory funnel into a dry bottle. Add 10–15 g. of anhydrous calcium chloride, stopper tightly with a cork, and allow to stand overnight to remove water and alcohol.

Through a funnel containing a small plug of cotton or glass wool, decant the dried ether into a 125–150-cc. distilling flask. Add a few chips of clay plate, adjust a thermometer, and connect the side-tube of the flask with a long water-cooled condenser. Heat on a water-bath or steam-bath and collect the ether boiling at 33-38° in a dry Erlenmeyer flask surrounded with an ice and salt mixture. Transfer the distilled product to a weighed bottle and stopper tightly with a cork. The yield is 40–50 g. Discard the small residue of alcohol and water which usually remains in the distilling flask.

➔ **Caution:** Ether has a high vapor tension and is extremely inflammable, and the vapor when mixed with air forms dangerously explosive mixtures. Take proper precautions against flames in carrying out this experiment and whenever ether is handled.

QUESTIONS

1. How do you account for the formation of sulfur dioxide and carbonaceous matter? What is formed if the temperature rises above 150°?

2. Why is the distillate washed with dil. sodium hydroxide solution? strong calcium chloride solution?

3. Compare the relative amounts of sulfuric acid and ethyl alcohol which are used in this experiment with those which are used in making ethylene, and give a reason for the difference.

4. Write equations showing a satisfactory method for preparing pure methyl *n*-butyl ether.

$CH_3COOH + C_4H_9OH \xrightarrow[H_2SO_4]{} CH_3COOC_4H_9$

Experiment 17

n-BUTYL ACETATE

In a 200-cc. round-bottom flask provided with a water-cooled reflux condenser, mix *thoroughly* 18.5 g. (23 cc.) of *n*-butyl alcohol (butanol-1), 19 g. (18 cc.) of glacial acetic acid and 3–4 g. (2 cc.) of concd. sulfuric acid. Reflux the mixture on an asbestos-centered wire-gauze for two hours. Cool the contents of the flask slightly, remove the condenser, set it downward for distillation, and connect it with the flask by means of a bent glass tube (about 8 mm. in diam.). Distil the reaction mixture until the residue in the distilling flask amounts to only a few cc. The distillate consists of butyl acetate, together with impurities of *n*-butyl alcohol, acetic acid, sulfurous acid, and water. Place the distillate in a 500-cc. flask, cool well by immersion in cold water or in an ice-bath, and add in small portions a saturated solution of sodium carbonate, until testing with blue litmus paper shows that the acid present is neutralized completely.

Transfer to a separatory funnel, remove the lower layer as completely as possible, and wash the *n*-butyl acetate layer with about 15 cc. of water. Separate the water and dry the *n*-butyl acetate with 6-8 g. of anhydrous magnesium sulfate (or 10–15 g. of Drierite). Decant through a funnel containing a small plug of cotton into a dry distilling flask. Add a few chips of clay plate, distil on an asbestos-centered wire-gauze, and collect in a weighed bottle the portion boiling at 119–125°. The yield is 20–22 g.

QUESTIONS

13.7 g.

1. What is the purpose of adding 2–3 cc. of concd. sulfuric acid in the preparation of *n*-butyl acetate? Would any *n*-butyl acetate be formed in the absence of the sulfuric acid?
2. Give two reasons why an excess of glacial acetic acid is used rather than the theoretical amount.
3. What is formed by the action of ammonia on *n*-butyl acetate?
4. Compare the reaction between *n*-butyl alcohol and acetic acid with the reaction between sodium hydroxide and hydrochloric acid.

Saponification of *n*-Butyl Acetate

In a 500-cc. round-bottom flask connected with a reflux condenser, place 15 g. of *n*-butyl acetate. To this add a solution of 50 per cent more than the calculated amount of solid sodium hydroxide, dissolved in about 200 cc. of water. Boil until the odor of *n*-butyl acetate can no longer be detected (about two hours). Set the condenser downward for distillation, distil off about 100 cc. of the liquid, and examine the distillate. What does it contain? Add enough clean salt (sodium chloride) to saturate the liquid (about 40–45 g. will be required), shake thoroughly, and allow to stand undisturbed for a short while.

Cool the residual solution in the flask and acidify with dil. sulfuric acid (about 10 per cent). Distil off about 75 cc. of liquid and examine the distillate. Test the odor and the reaction toward litmus paper. What does the solution contain? How could you isolate this substance in an almost pure state?

Organic acids vary widely in the rate at which they can be esterified by the procedure just described. Those with the carboxyl attached to a tertiary carbon are especially difficult to esterify in this manner. Alternative methods for preparing esters, therefore, are preferable in such cases: (1) conversion of the acid to the corresponding acid chloride, followed by treatment with an alcohol; (2) conversion of the acid to the sodium, potassium, or silver salt, followed by treatment with an alkyl halide (using a little secondary amine as a catalyst).

$$\mathrm{RCOOH} \longrightarrow \mathrm{RCOCl} \xrightarrow{\mathrm{R'OH}} \mathrm{RCOOR'}$$

$$\mathrm{RCOOH} \longrightarrow \mathrm{RCOONa} \xrightarrow{\mathrm{R'X}} \mathrm{RCOOR'}$$

Esters of tertiary acids are less readily saponified than esters of secondary or primary acids. Where difficulty in saponification is encountered, due either to the type of structure of the molecule or to the fact that the ester is very insoluble in water, it is advantageous to use potassium hydroxide dissolved in methyl or ethyl alcohol containing 5–10 per cent of water.

QUESTIONS

1. Why is the hydrolysis of an ester with alkalies called saponification?
2. What would be formed by the action of hot dil. sulfuric acid upon *n*-butyl acetate? Write the equation, and explain why it is preferable to carry out this reaction with sodium hydroxide solution.

Experiment 18

FATS AND FATTY OILS

Preparation and Properties of Soap. Place 12 g. of lard (or any fat or fatty oil) in a 150-cc. beaker and add a solution of 5 g. of solid sodium hydroxide in 15 cc. of distilled water, and 10 cc. of alcohol. Stir the mixture thoroughly and warm gently on an asbestos-centered wire-gauze over a very small flame. Continue to heat the mixture very gently so that it boils without spattering. As the alcohol and water boil away, add more from time to time so that the volume remains about constant. For this purpose prepare a mixture of 25 cc. of alcohol and 25 cc. of distilled water. Do not allow the mixture to boil dry, and stir to avoid spattering. If material spatters on the side of the beaker, push the substance back into the solution with a glass rod.

After about forty minutes of heating, the saponification is complete (as shown by the absence of the odor of fat and of oily globules). Pour the hot solution containing soap, glycerol, excess sodium hydroxide, and alcohol, into about 300 cc. of a filtered saturated salt (sodium chloride) solution and 50 cc. of water. Filter the precipitated soap with suction, and wash twice with 5-cc. portions of *ice-cold* distilled water.

Prepare a solution of about 1 g. of soap in 100 cc. of warm distilled water, and perform the following tests:

(a) Add a few drops of dil. hydrochloric acid to about 10 cc. of the clear soap solution and cool. What is the precipitate? Test the lathering property of the acid solution. Add 2–3 cc. of dil. sodium hydroxide solution and test again.

(b) To about 5 cc. of the clear soap solution in a series of four test-tubes, add 2–3 drops of a 10 per cent aqueous solution of the following inorganic salts: calcium chloride; magnesium chloride; ferric chloride; potassium chloride. Record your observations.

(c) Mix about 10 cc. of clear soap solution with an equal volume of tap water and shake well. Explain the action of hard water.

(d) *Emulsification Test.* To 5 cc. of clear soap solution add 4 drops of cottonseed oil, shake well, and allow to stand. Does the oil

separate? Carry out similar tests with 5 cc. of each of the following, instead of the soap solution: dil. sodium hydroxide, dil. hydrochloric acid, water.

Unsaturation Test. Dissolve 2–3 cc. of cottonseed or linseed oil in about 5 cc. of carbon tetrachloride and add drop by drop, a solution of bromine in carbon tetrachloride. Repeat the test with 1 g. of lard or Crisco.

Drying Oils. In a test-tube place 3–4 cc. of linseed oil, add a small pinch (about 0.1 g.) of litharge (PbO) and boil the mixture gently for about ten minutes. Pour the hot mixture into a watch glass, allow to stand for several hours, and observe.

Linseed oil from flaxseed, and tung oil (China wood oil) from the seeds of an oriental tree are two of the most important oils used in paint and varnish manufacture, and furnish in large part the quick drying quality to the products. They differ from many of the vegetable oils in containing a substantial proportion of glycerides of fatty acids having two or more double bonds.

Fish oils are sources of valuable vitamins and can also be converted by partial or complete hydrogenation into fats suitable for various commercial purposes. Generally the fish oils are more highly unsaturated than common animal fats and oils, and contain a larger proportion of higher fatty acids (C_{20}, C_{22}, etc.).

Glycerides of hydroxy acids are present in a few commercial vegetable oils. The most important of these is castor oil, which consists mainly of the glyceride of ricinoleic acid (12-hydroxy-9,10-octadecenoic acid):

$$CH_3—(CH_2)_5—CHOH—CH_2—CH{=}CH—(CH_2)_7—CO_2H$$

In recent years a variety of synthetic compounds possessing powerful detergent properties have been developed as substitutes for soap. The commercial synthetic detergents are generally sodium salts of long-chain alkyl sulfates [*e.g.*, $CH_3—(CH_2)_{10}—CH_2—O—SO_2—ONa$] or long-chain aliphatic sulfonic acids [*e.g.*, $CH_3—(CH_2)_{14}—CH_2—SO_2—ONa$], containing either straight or branched chain structures. These synthetic materials are active detergents in very dilute solutions and have an important advantage over ordinary soap; they do not give precipitates with hard water, since their magnesium, calcium, and heavy metal salts are appreciably soluble in water.

QUESTIONS

1. How may the glycerol from a saponification be isolated? Mention several important commercial uses of glycerol.
2. What is the iodine number of a fatty oil? What information does it give concerning the glycerides present?
3. What chemical processes occur during the drying of linseed oil?

Experiment 19

ACETYL CHLORIDE

It is important to have all apparatus used in this preparation perfectly dry, since both acetyl chloride and phosphorus trichloride are decomposed by water.

Connect a dry 100–125-cc. distilling flask with a water-cooled condenser set downward for distillation. For the receiver attach to the lower end of the condenser by means of a tightly fitting cork, a dry 100–125-cc. distilling flask (or a suction filtering flask) and provide the side-tube with a calcium chloride tube half-filled with anhydrous calcium chloride, to protect the distillate from moisture. By means of a cork holding a glass tube, connect the open end of the calcium chloride tube to a funnel inverted *over* 200–300 cc. of water in a beaker which serves to absorb the hydrogen chloride formed due to secondary reactions. The funnel must not dip below the surface of the water, or the latter may be drawn up into the dry apparatus.

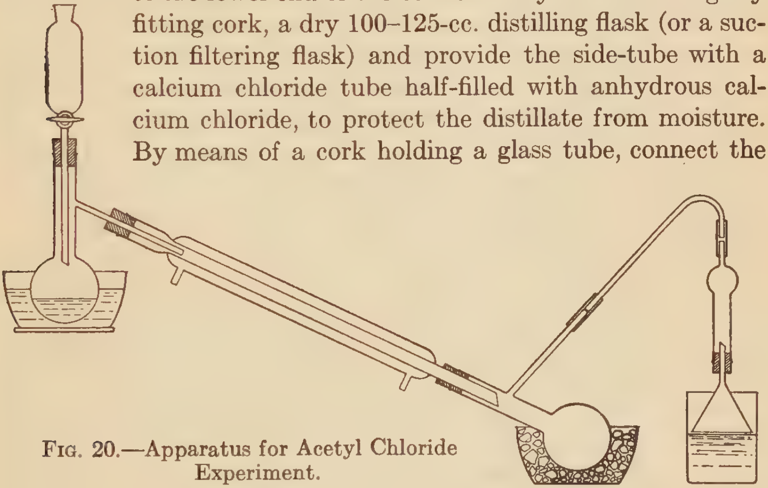

Fig. 20.—Apparatus for Acetyl Chloride Experiment.

Place 24 g. (23 cc.) of glacial acetic acid in the distilling flask, close with a cork holding a separatory funnel, and add slowly through the funnel 21 g. (13 cc.) of phosphorus trichloride. Keep

➔ **Caution:** Do not allow phosphorus trichloride or acetyl chloride to come in contact with the skin. These substances produce dangerous burns which heal very slowly.

the flask cool by immersion in a water-bath. Mix thoroughly and after allowing the mixture to stand for ten minutes, heat in a water-bath maintained at 40–50° for thirty minutes. The liquid which was homogeneous before heating may separate into two layers.

Distil the acetyl chloride (which forms the upper layer) by heating the water-bath to boiling and maintaining it at that temperature as long as anything passes over. It is advantageous to cool the receiver in an ice-bath during the distillation. The syrupy residue in the distilling flask is phosphorous acid, which is discarded. To the distillate add *two drops* of glacial acetic acid (to destroy phosphorous esters that would cause turbidity to develop on standing) and then redistil the acetyl chloride from a distillation apparatus arranged as above, except that the separatory funnel is replaced by a thermometer. Collect separately in a dry receiver the portion which boils at 50–56° and transfer to a dry weighed glass-stoppered bottle (acetyl chloride attacks corks and rubber stoppers). The yield is 20–24 g.

Reactions of Acid Chlorides

$HCl + CH_2COOH$

(A) Add cautiously a few drops of acetyl chloride to about 5 cc. of water in a test-tube, and observe the result.

(B) Place about 2 cc. of ethyl alcohol in a test-tube and add drop by drop, about 2 cc. of acetyl chloride, keeping the mixture cooled by running water. Now add about 2 cc. of a saturated solution of salt (sodium chloride) and observe the result. Note the odor of the product.

(C) Add cautiously drop by drop about 1 cc. of acetyl chloride to about 1 cc. of aniline. After the vigorous reaction is over, dilute the reaction mixture with 15–20 cc. of water and note the result. What is this substance? [illegible]

QUESTIONS

1. How do the physical characteristics of the acid chlorides compare with those of the acids from which they are derived?
2. Mention another reagent which is used for preparing acid halides from acids.
3. Write the equation for the reaction between acetyl chloride and ammonia.
4. Show by an equation how acetyl chloride may be converted into acetic anhydride.

Experiment 20

ACETAMIDE

Place 50 g. of ammonium acetate in a 200-cc. round-bottom flask and add 42 g. (40 cc.) of glacial acetic acid. Provide the flask with a short fractionating column leading to a condenser set downward for distillation. Add a few chips of clay plate and heat the flask on an asbestos-centered wire-gauze, so that the mixture boils very gently and the vapors do not rise into the fractionating column. After the mixture has boiled gently for one hour, increase the heating slightly so that the water formed in the reaction and a part of the acetic acid distil off *very slowly at a uniform* rate.[1] It is convenient to observe and control the rate of distillation by using a small graduated cylinder as the receiver.

During the first hour of distillation the temperature of the distilling vapor should not rise above 104–105°, and at the end of the hour the volume of distillate should not exceed 12–14 cc. After the first hour the vapor temperature rises gradually to about 118°, as the distillation progresses. Continue the fractionation very slowly and at a uniform rate, until the total distillate amounts to 50 cc.

Allow the residual acetamide in the flask to cool somewhat, and transfer to a small dry distilling flask attached to an air-cooled condenser, set downward for distillation. Add a few chips of clay plate and continue the distillation. Collect the following fractions: (A) up to 195°, (B) 195–215°, (C) 215–225°. The fractions (B) and (C) will usually solidify completely or in part upon cooling. If either fraction does not solidify completely upon cooling, filter with suction the mixture of liquid and solid, and press the crystals as dry as possible on the filter paper. Combine the crystalline products from (B) and (C), pulverize the crystals, and place them quickly in a dry weighed bottle, since acetamide is somewhat hygroscopic. The liquid portion may be combined with fraction

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[1] The success of this preparation depends upon careful fractionation to remove the water and acetic acid, without loss of ammonium acetate or acetamide. The desired result cannot be achieved by rapid, careless fractionation.

(A) and refractionated to obtain an additional quantity of acetamide. The yield is 20–25 g.

Recrystallize 2–3 g. of crude acetamide from a mixture of 3 cc. of benzene and 1 cc. of ethyl acetate. Warm in a test-tube on the water-bath until all is dissolved, and cool rapidly in an ice-bath. Filter, press the crystals between filter papers, dry in a desiccator, and determine the melting-point.

Carry out the *Reactions of Acid Amides* with the crude acetamide, and turn in the remainder.

Reactions of Acid Amides

(A) Boil a small quantity (about 1 g.) of acetamide with about 5 cc. of strong sodium hydroxide solution (about 20 per cent) and note the odor of the vapor that is evolved.

(B) Boil a small quantity (about 1 g.) of acetamide with about 5 cc. of dil. sulfuric acid (10 per cent) and note the odor of the vapor that is evolved.

(C) Dissolve a gram of acetamide in 2–3 cc. of water, add a *small pinch* of yellow mercuric oxide, and warm gently. A water-soluble mercury derivative, $(CH_3—CO—NH)_2Hg$, is formed.

The conversion of acetic acid to acetamide illustrates a general process known as ammonation or ammonolysis. These reactions of ammonia are analogous to the well-known reactions of hydration and hydrolysis, with ammonia in place of water.

An exceedingly important group of natural products, the proteins, contain nitrogen in the form of amide linkings (called in this special case, peptide linkages). The proteins are poly-amides of exceedingly high molecular weight, containing a large number of α-amino-acid units held together in amide combinations. The type of these amides is illustrated by the dipeptide derived from two molecules of aminoacetic acid ($NH_2—CH_2—CO_2H$): $NH_2—CH_2—\underset{\text{peptide linkage}}{CO—NH}—CH_2—CO_2H$

In a protein, hundreds of amino-acid units are combined in this way.

QUESTIONS

1. What products would be formed upon heating methylammonium acetate in place of ammonium acetate in the above experiment?
2. Write equations illustrating two other methods of preparing acetamide.
3. Write equations illustrating the action of the following reagents upon acetamide: sodium hypobromite solution; phosphorus pentoxide.
4. Compare the relative volatility of $R—CO_2H$, $R—CO—OCH_3$, $R—CO—Cl$, $R—CO—NH_2$, and $R—C{\equiv}N$, where R— is a simple alkyl group.

Experiment 21

ACETONITRILE (METHYL CYANIDE)

In a dry 100–150-cc. distilling flask place 30 g. of phosphorus pentoxide, and add 20 g. of dry, pulverized acetamide. Shake thoroughly to mix the two solids and connect the side-tube of the flask with a short water-cooled condenser (25–30 cm. in length), set downward for distillation. At the lower end of the condenser, arrange a large test-tube or a small flask to serve as receiver. Carefully heat the flask directly with a small yellow flame; hold the burner in the hand and keep the flame in constant motion. The reaction mixture foams during the heating.

After the mixture has been heated for five or six minutes, distil the acetonitrile with a luminous flame as before and collect the distillate in the receiver. Treat the distillate with half its volume of distilled water, and add solid anhydrous potassium carbonate in small portions until the aqueous layer is saturated (about 8–9 g. of potassium carbonate will be required for every 10 cc. of water). Cool the tube in a bath of ice-water during the addition of potassium carbonate to prevent loss of acetonitrile by evaporation.

Allow the excess of solid potassium carbonate to settle, and decant the liquid into a small separatory funnel. Draw off and discard the lower aqueous layer. Transfer the upper layer of methyl cyanide through the mouth of the funnel to a very small distilling flask and add 0.5–1.0 g. of phosphorus pentoxide as a drying agent. Add a few chips of clay plate, distil on an asbestos-centered wire-gauze, and collect in a weighed bottle the portion boiling at 79–82°. The yield is 8–10 g.

➔ **Caution:** Phosphorus pentoxide is extremely hygroscopic and must be kept out of contact with the air. It must be handled carefully since it will produce painful burns if allowed to come in contact with the skin.

QUESTIONS

1. Why is methyl cyanide also called acetonitrile?
2. Write equations for another method of preparing nitriles.
3. Show by means of equations the action of the following reagents on acetonitrile: hot dil. sulfuric acid; hot dil. sodium hydroxide solution.

Experiment 22a

FORMALDEHYDE (METHANAL)

Prepare a closely wound spiral of copper wire (by winding the wire around a glass tube) and oxidize it by heating in the oxidizing flame of a Bunsen burner. Plunge the spiral while still red-hot into a test-tube containing a mixture of about 1 cc. of methyl alcohol and 5 cc. of water. Stopper the test-tube loosely, cool, remove the spiral, and repeat the oxidation twice in the same manner. Note the odor of the solution. Filter and test the solution for the presence of formaldehyde according to (A) and (D).

(A) In a thoroughly clean test-tube, place about 5 cc. of an ammoniacal silver oxide solution (prepared as described below). Add a few drops of the oxidized methyl alcohol solution and warm gently. If the test-tube is not thoroughly clean, a precipitate of black, finely divided silver is obtained instead of a mirror.

Preparation of an Ammoniacal Solution of Silver Oxide (Tollens' Reagent). In a thoroughly clean test-tube place 2 cc. of a 5 per cent solution of silver nitrate, and add a drop of dil. sodium hydroxide solution (10 per cent). Add a very dilute solution of ammonia (about 2 per cent) drop by drop, with constant shaking, until the precipitate of silver oxide just dissolves. In order to obtain a sensitive reagent it is necessary to avoid a large excess of ammonia.

This reagent should be freshly prepared just before use and should not be stored, since the solution decomposes on standing and deposits a highly explosive precipitate.

(B) Dilute a few drops of strong formaldehyde solution (40 per cent) with water, add about 5 cc. of a dil. solution of sodium hydroxide (10 per cent), and boil for a few minutes. Write an equation to indicate what products are formed.

(C) To about 1 cc. of strong formaldehyde solution (40 per cent) contained in a small evaporating dish, add an excess (about 2 cc.) of concd. aqueous ammonia and evaporate to dryness on a water-bath or steam-bath. The white solid which is left is hexamethylenetetramine.

Notice that the reactions of formaldehyde with sodium hydroxide and ammonia are unlike those which take place with other aliphatic aldehydes.

(D) **Milk Test for Formaldehyde.** In a test-tube place about 5 cc. of milk, add an equal volume of water and a drop or two of ferric chloride solution (about 10 per cent). Incline the tube at an angle and pour 5–6 cc. of concd. sulfuric acid down the side of the tube so that it forms a layer on the bottom, and does not mix with the milk. If formaldehyde is present a violet ring is formed at the juncture of the two liquids. It is sometimes necessary to warm the tube in a water-bath to bring about the development of the violet color. Do not mistake a brown coloration for the violet ring which is given by formaldehyde. This violet coloration is due to a reaction between formaldehyde and one of the constituents of the milk (presumably a protein containing tryptophane). Formaldehyde was formerly used to preserve milk, but its use is now prohibited by law.

Add a drop of the oxidized methyl alcohol solution to a sample of pure milk and repeat the above test.

The carbonyl group of formaldehyde is more reactive than that of other aldehydes, and as a consequence formaldehyde undergoes a number of reactions that occur difficultly (or not at all) with other carbonyl compounds. With molecules containing an active hydrogen it reacts to form, at first, hydroxymethyl (methylol) derivatives. Urea, a bifunctional acid amide, reacts with excess formaldehyde to give a crystalline dimethylolurea:

$$NH_2—CO—NH_2 + 2CH_2{=}O \longrightarrow HOCH_2—NH—CO—NH—CH_2OH$$

On heating, the latter undergoes polymerization to form a colorless transparent plastic material that is used commercially as a "non-breakable glass." Formaldehyde reacts with phenol (C_6H_5—OH) to form hydroxymethyl derivatives that can be polymerized by heating and yield synthetic resins having a variety of uses ("Bakelite" resins).

QUESTIONS

1. How is formaldehyde made commercially? What are some of the important uses for formaldehyde?
2. What are some of the important uses for hexamethylenetetramine?
3. Write equations to show what is formed when formaldehyde is reduced with hydrogen; oxidized further.
4. How do you account for the fact that formaldehyde differs from the other aliphatic aldehydes in its behavior toward several important reagents?

Experiment 22b

ACETALDEHYDE (ETHANAL)

Provide a 200-cc. round-bottom flask with a fractionating column having at least two bulbs. Fit the column with a cork holding a thermometer, and connect the side-tube to a long water-cooled condenser (60–70 cm. in length) set downward for distillation. By means of a cork, attach an adapter to the lower end of the condenser tube and use a 100–150-cc. Erlenmeyer flask as a receiver. Cool the receiver in an ice-bath, but not in an ice and salt mixture. A *loose* plug of cotton between the condenser tube and the receiver will also diminish the evaporation losses. Care must be taken to prevent the cotton from coming in contact with the distillate.

In the 200-cc. round-bottom flask, place 20 g. (20 cc.) of paraldehyde and add 4–5 drops of concd. sulfuric acid, or some other suitable depolymerizing agent (see below). Support the flask on an asbestos-centered wire-gauze and heat gently with a small flame, so that the temperature of the vapors which distil does not rise above 35°. Avoid overheating since this may cause carbonization and formation of sulfur dioxide, which will cause the acetaldehyde to repolymerize in the distillate. Continue to heat the flask and collect about 10–12 cc. of distillate, which is practically pure acetaldehyde. Stopper the flask loosely with a cork, keep it in the ice-bath, and draw out small portions for the tests below.

Depolymerizing Agents. The small amount of sulfuric acid acts catalytically and causes the depolymerization of paraldehyde. The 4–5 drops of sulfuric acid may be replaced advantageously by 1–2 g. of sulfamic acid ($NH_2—SO_3H$) or *p*-toluenesulfonic acid ($CH_3—C_6H_4—SO_3H$). These acids do not cause carbonization so easily as sulfuric acid, and thus reduce the danger of liberating sulfur dioxide. If sulfur dioxide is formed it causes the acetaldehyde in the distillate to repolymerize.

(A) In a test-tube place 1–2 cc. of pure acetaldehyde, treat cautiously with a drop of concd. sulfuric acid, mix well, and observe the change in temperature. Add 3–4 cc. of water and observe the result. What is the insoluble product?

(B) **Fehling's Test.** In a test-tube place about 10 cc. of freshly prepared Fehling's solution [made by mixing equal volumes of Fehling's solution No. 1 (copper sulfate solution) and solution No. 2 (alkaline tartrate solution)] or 10 cc. of Benedict's solution. Add one or two drops of acetaldehyde, boil the solution gently for two or three minutes, and observe the result.

Preparation of Fehling's Solution. Fehling's solution is made by mixing together, at the moment when it is to be used, equal volumes of a solution of copper sulfate (called Fehling's solution No. 1) and an alkaline solution of sodium potassium tartrate (called Fehling's solution No. 2). For qualitative work these solutions may be prepared as follows: (No. 1), dissolve 3.5 g. of pure copper sulfate crystals ($CuSO_4$, $5H_2O$) in 100 cc. of water; (No. 2), dissolve 17 g. of sodium potassium tartrate crystals (Rochelle salt) in 15–20 cc. of warm water, add a solution of 5 g. of solid sodium hydroxide in 15–20 cc. of water, cool, and dilute to a volume of 100 cc. The solutions are kept separately and not mixed until time for use, since the mixed solution deteriorates on standing.

Benedict's Solution. Benedict has modified Fehling's solution and devised a single test solution that does not deteriorate on standing. For qualitative work this solution may be prepared as follows: Dissolve 20 g. of sodium citrate and 11.5 g. of anhydrous sodium carbonate in 100 cc. of hot water in a 400-cc. beaker. Add slowly to the citrate-carbonate solution, with continual stirring, a solution of 2 g. of copper sulfate crystals in 20 cc. of water. The mixed solution should be perfectly clear (if not, pour it through a fluted filter).

(C) In a *thoroughly clean* test-tube, place about 5 cc. of ammoniacal silver oxide solution (prepared as described below). Add a drop or two of acetaldehyde, mix thoroughly, and warm gently. If a silver mirror is not formed on the walls of the tube, add a drop of dil. sodium hydroxide solution (10 per cent) and warm again. If the test-tube is not thoroughly clean a precipitate of black, finely divided silver is obtained instead of a mirror.

Preparation of an Ammoniacal Solution of Silver Oxide (Tollens' Reagent). In a thoroughly clean test-tube place 2 cc. of a 5 per cent solution of silver nitrate, and add a drop of dil. sodium hydroxide solution (10 per cent). Add a very dilute solution of ammonia (about 2 per cent) drop by drop, with constant shaking, until the precipitate of silver oxide just dissolves. In order to obtain a sensitive reagent it is necessary to avoid a large excess of ammonia.

This reagent should be freshly prepared just before use and should not be stored, since the solution decomposes on standing and deposits a highly explosive precipitate.

(D) In a test-tube add a drop of acetaldehyde to about 5 cc. of a dil. solution of sodium hydroxide (10 per cent) and boil for a few minutes. Compare the result with that obtained when formaldehyde was similarly treated in a previous experiment.

(E) **Schiff's Fuchsin-Aldehyde Test.** Add a drop of acetaldehyde to 4–5 cc. of water, and to the solution add about 1 cc. of fuchsin-aldehyde reagent. Ketones do not give this test when perfectly pure, but the color reaction is very sensitive and will appear if mere traces of an aldehyde are present. Try the test with a drop of acetone, or other ketone (methyl amyl ketone, acetophenone, etc.).

Preparation of Schiff's Fuchsin-Aldehyde Reagent. Dissolve 0.5 g. of pure fuchsin (*p*-rosaniline hydrochloride) in 500 cc. of distilled water, and filter the solution. Saturate 500 cc. of distilled water with sulfur dioxide, mix thoroughly with the filtered fuchsin solution, and allow to stand overnight. This produces a practically colorless and very sensitive reagent.

(F) Observe the color, odor, and solubility in water, of pure acetaldehyde.

(G) Acetaldehyde when allowed to stand in an ice-bath often polymerizes spontaneously to metaldehyde, a white crystalline substance. Examine for such precipitate the remainder of the distillate which has been standing in the freezing mixture. If no metaldehyde has deposited it may often be made to form by adding a lump of anhydrous calcium chloride to the ice-cold sample and allowing it to stand for some time at a low temperature, especially in an ice and salt mixture. Do not attempt to conserve a sample of acetaldehyde from one laboratory period to another.

QUESTIONS

1. Write equations indicating a series of reactions by means of which acetaldehyde may be prepared from coke (carbon).
2. Write equations to show what is formed when acetaldehyde is reduced with hydrogen; oxidized further; treated with phosphorus pentachloride.
3. Define the terms: empirical formula; molecular formula; isomer; polymer (see page 369).
4. Write equations illustrating the aldol condensation and formation of crotonaldehyde from acetaldehyde.
5. What product is obtained by catalytic hydrogenation of crotonaldehyde?

Experiment 23

CYCLOHEXANONE

In a 400-cc. beaker, place 42 g. of sodium dichromate dihydrate (or 41 g. of potassium dichromate) and 200 cc. of water. Add carefully 35 g. (19 cc.) of concd. sulfuric acid, with stirring, and cool the deep orange-red solution to 30°. Place 20 g. (21 cc.) of cyclohexanol (technical grade) in a 500-cc. Erlenmeyer flask and *to it* add the dichromate solution in one portion. Shake the mixture to insure thorough mixing and observe its temperature with a thermometer. The mixture rapidly becomes warm; when the temperature reaches 55° cool the flask in a basin of cold water, or under the tap, and regulate the amount of cooling so that the temperature does not rise above 60° nor fall below 55°. Continue external cooling only so long as it is necessary to maintain this temperature; when the temperature of the mixture no longer rises above 60° on removal of external cooling, allow the flask to stand on the desk, with occasional shaking, for one hour.

Pour the mixture into a 1-l. round-bottom flask, add an additional 200 cc. of water, and attach a condenser set downward for distillation. Distil the mixture until about 100 cc. of distillate, consisting of water and an upper layer of cyclohexanone, has been collected. Saturate the aqueous layer with salt (20–25 g. will be required), separate the cyclohexanone layer, and extract the aqueous layer with 20 cc. of ether. Combine the ether extract with the cyclohexanone layer and dry with 5–6 g. of anhydrous magnesium sulfate. Filter the dried ether solution into a distilling flask of suitable size (50-cc. is convenient), attach a condenser and distil off the ether from a water-bath. Distil the residual cyclohexanone, using an asbestos-centered wire-gauze, and collect the fraction boiling at 150–155° (mainly 152–154°). The yield is 12–13 g.

QUESTIONS

1. Compare the three classes of alcohols in their behavior toward mild oxidizing agents.
2. What is formed by vigorous oxidation of cyclohexanone with nitric acid?

Experiment 24

REACTIONS OF THE CARBONYL GROUP IN ALDEHYDES AND KETONES

(A) **Sodium Bisulfite Reaction.** *Butyraldehyde.* In a 100–150-cc. Erlenmeyer flask place 10 cc. of a *saturated* solution of sodium bisulfite and add slowly 4 g. (5 cc.) of *n*-butyraldehyde (freshly distilled). Shake thoroughly to complete the reaction. After several minutes add about 50 cc. of alcohol, shake well, and chill thoroughly in an ice and salt mixture. The sodium bisulfite addition compound crystallizes in shining white plates. Filter with suction, wash with alcohol, finally with ether, and allow to dry. Do not attempt to determine the melting-point of this metallic salt.

Treat a small amount of the sodium bisulfite addition compound with 5–10 cc. of sodium carbonate solution (10 per cent) and warm. Note the odor. Repeat with 5–10 cc. of dil. hydrochloric acid in place of sodium carbonate solution and cautiously test the odor.

Acetone and Sodium Bisulfite. Add 4 g. (5 cc.) of acetone drop by drop to 10 cc. of a *saturated* solution of sodium bisulfite contained in a beaker immersed in an ice-bath. Shake thoroughly and allow to crystallize. After a few minutes add about 25 cc. of alcohol to promote the precipitation. Filter the crystals with suction, wash with alcohol, finally with ether, and allow to dry. Do not attempt to determine the melting-point.

Treat a small amount of the sodium bisulfite addition compound with 5–10 cc. of sodium carbonate solution (10 per cent) and warm. Note the odor. Repeat with 5–10 cc. of dil. hydrochloric acid in place of sodium carbonate solution and cautiously test the odor.

(B) **Formation of Oximes.** *Acetone and Hydroxylamine.* In a small Erlenmeyer flask mix together 5 g. of hydroxylamine sulfate (or hydroxylamine hydrochloride) dissolved in 10 cc. of water, 3 g. of sodium hydroxide dissolved in 10 cc. of water, and add 6.5 g. (8 cc.) of acetone. Cork the flask firmly, shake thoroughly,

and leave overnight, during which time the crystalline oxime separates. If no crystals appear, scratch the inside of the flask with a glass rod and at the same time cool in an ice-bath; or add a seed-crystal of the oxime and allow to stand again. Filter the crystals with suction, dry quickly, and take the melting-point. Do not leave acetoxime exposed to the air overnight as it sublimes readily. Boil a little acetoxime with 5–10 cc. of dil. hydrochloric acid and note the odor.

Cyclohexanone Oxime. Dissolve 5 g. of hydroxylamine sulfate (or hydrochloride) and 7.5 g. of sodium acetate crystals ($NaC_2H_3O_2,3H_2O$) in 20 cc. of water in a 50-cc. Erlenmeyer flask. Warm the solution to about 40° and add 5 g. (5.3 cc.) of cyclohexanone. Stopper the flask securely with a softened cork and shake it vigorously for a few minutes. The oxime separates as a crystalline solid. Cool the flask in an ice-bath, filter the crystals with suction, and wash with a little ice-cold water. Press as dry as possible on the funnel, spread the product on a piece of filter paper to dry in the air, and take the melting-point. The yield is 4.5–5 g. The recorded melting-point of cyclohexanone oxime is 89–90°.

Furfural may be converted to the oxime by the first procedure, using instead of acetone, a suspension of 5.5 g. (5 cc.) of furfural in 10 cc. of water. Furfuraldoxime exists in two isomeric forms, geometrical isomers, having different physical properties (α-, m.p. 73–74°; β-, m.p. 89°). The β-form is usually obtained by the oximation procedure given above.

Many aldehydes and ketones give oximes that are liquids at ordinary temperatures (*e.g.*, *n*-butyraldehyde, methyl ethyl ketone), or are very difficult to obtain in crystalline form. For such compounds the semicarbazones are likely to be suitable crystalline derivatives for characterization.

(C) **Semicarbazones.** *n-Butyraldehyde semicarbazone.* Prepare a solution of 1 g. of semicarbazide hydrochloride ($NH_2—CO—NH—NH_2, HCl$) and 1.5 g. of sodium acetate crystals in 10 cc. of water, in a test-tube. Add 1 g. (1 cc.) of *n*-butyraldehyde, close the tube with a cork, and shake vigorously. Allow the mixture to stand, with occasional vigorous shaking, until the product has crystallized completely (cool in an ice-bath if necessary, to promote crystallization). Filter the crystals, wash with a little cold water, and dry in the air. Take the melting-point. The recorded melting-point of this semicarbazone is 106°.

Acetone, furfural, cyclohexanone, etc., may be converted to crystalline semicarbazones[1] in the same manner. For less reactive carbonyl compounds it is advantageous to heat the reaction mixture for a few minutes in a beaker of boiling water. For water-insoluble carbonyl compounds, dissolve 1 g. of the substance in 10 cc. of ethyl alcohol, add water dropwise until the solution becomes turbid, then add 1 g. of semicarbazide hydrochloride and 1.5 g. of sodium acetate crystals. Shake vigorously, and warm to 100° if necessary.

(D) **Phenylhydrazones.** *Furfural Phenylhydrazone.* Prepare a solution of phenylhydrazine reagent[2] by dissolving 2 g. of phenylhydrazine hydrochloride (C_6H_5—NH—NH_2,HCl) in 18 cc. of water, and adding 3 g. of sodium acetate crystals and one drop of glacial acetic acid. If the resulting solution is turbid, add a *small pinch* of decolorizing charcoal, shake vigorously, and filter. This reagent deteriorates rapidly and should not be stored.

Divide the solution into two equal portions, and to one-half add a solution of $\frac{1}{2}$ cc. of furfural (C_4H_3O—CH═O) in 6–8 cc. of water. Cork the tube and shake vigorously until the product has crystallized. Filter the crystals with suction (do not allow them to stand overnight, as discoloration occurs readily), and wash thoroughly with water. Recrystallize from dil. alcohol, dry the crystals as quickly as possible, and take the melting-point. The recorded melting-point of furfural phenylhydrazone is 97°.

Cyclohexanone Phenylhydrazone. To the other half of the phenylhydrazine reagent, add a solution of $\frac{1}{2}$ cc. of cyclohexanone in 6–8 cc. of water. Isolate the phenylhydrazone in the same way, recrystallize from dil. alcohol, and take the melting-point. The recorded melting-point of this phenylhydrazone is 77°.

QUESTIONS

1. What is a cyanohydrin? How may acetone cyanohydrin be prepared?
2. What is an acetal? Indicate by equations a method of preparing the diethyl acetal of *n*-butyraldehyde.
3. What tests may be used to distinguish between aldehydes and ketones?

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[1] The recorded melting-points of these semicarbazones are: acetone, 187°; furfural, 202°; cyclohexanone, 166°.

[2] A satisfactory reagent may also be made by dissolving 2 g. (2 cc.) of phenylhydrazine (the free base is a liquid) in a solution of 2 g. (2 cc.) of glacial acetic acid in 20 cc. of water, and clarifying with a little decolorizing charcoal. This procedure is less desirable owing to the poisonous character of phenylhydrazine (vapor or liquid). If the liquid comes in contact with the skin it must be washed off at once, using 5 per cent acetic acid, followed by soap and water.

Experiment 25

IODOFORM (TRIIODOMETHANE)

In a 1-l. round-bottom flask place a solution of 12.5 g. of potassium iodide in 250 cc. of water, and add 2.5 g. (3 cc.) of acetone. To this solution, with frequent shaking, add from a separatory funnel, a dil. solution of sodium hypochlorite [1] ("Clorox") as long as any precipitate is formed. Allow the crystalline precipitate to settle, decant the liquid, and wash the crystals two or three times with water. Filter with suction and press the crystals as dry as possible on the filter.

Purify the crude iodoform in the following way. Dissolve the product in slightly more than the necessary amount of hot alcohol and filter the hot solution to remove insoluble impurities. To the filtrate add water until the iodoform is completely precipitated as light yellow crystals. Cool thoroughly, filter with suction, and allow the crystals to dry. The yield is 6–8 g.

The formation of iodoform is an example of the haloform reaction, which is typical of methyl ketones (CH_3-CO-R) and of secondary alcohols of the type $CH_3-CHOH-R$. Only one aldehyde ($CH_3-CH=O$) and only one primary alcohol (CH_3-CH_2OH) give a positive haloform reaction.

QUESTIONS

1. Write equations showing how iodoform could be obtained by using ethyl alcohol in place of acetone in the above experiment.
2. Which of the following alcohols would give iodoform by the above experimental procedure: *n*-propyl alcohol? isopropyl alcohol? *n*-butyl alcohol? isobutyl alcohol? *sec*-butyl alcohol (butanol-2)? Give the reasons for your answers.
3. Write structural formulas for two ketones other than acetone which would give iodoform in the above experiment.
4. Write equations showing how bromoform could be prepared from ethyl alcohol.

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[1] A stabilized solution of sodium hypochlorite (5 per cent) sold at most grocery stores under the name "Clorox," is quite satisfactory for this preparation. About one-third (160 cc.) of a one-pound bottle (costing about twenty cents) is required in this experiment.

Experiment 26

CARBOHYDRATES—SUGARS

(a) Monosaccharides

Glucose (*d*-Glucose, Grape Sugar, Dextrose) $C_6H_{12}O_6 + H_2O$. Prepare a solution of 1 g. of pure glucose in 50 cc. of disilled water and use this solution in the following experiments. Briefly describe and explain each result, using equations wherever possible.

(A) **Fehling's Test for Reducing Sugars.** In a test-tube place about 10 cc. of Fehling's solution [made by mixing equal volumes of Fehling's solution No. 1 (copper sulfate solution) and solution No. 2 (alkaline tartrate solution)] or 10 cc. of Benedict's solution. Heat the solution to gentle boiling and add 2–3 drops of the glucose solution. Continue to boil gently and observe the result after a minute or two. Continue to add the glucose solution, 2–3 drops at a time, and heat for a short while after each addition, until the deep blue color just disappears. Fehling's solution contains a known amount of copper per cc. of solution; suggest a method for determining the amount of glucose in a solution of unknown strength.

Preparation of Fehling's Solution. Fehling's solution is made by mixing together, at the moment when it is to be used, equal volumes of a solution of copper sulfate (called Fehling's solution No. 1) and an alkaline solution of sodium potassium tartrate (called solution No. 2). For qualitative work these solutions may be prepared as follows: (No. 1), dissolve 3.5 g. of pure copper sulfate crystals ($CuSO_4,5H_2O$) in 100 cc. of water; (No. 2), dissolve 17 g. of sodium potassium tartrate crystals (Rochelle salt) in 15–20 cc. of warm water, add a solution of 5 g. of solid sodium hydroxide in 15–20 cc. of water, cool, and dilute to a volume of 100 cc. The solutions are kept separately and not mixed until time for use, since the mixed solution deteriorates on standing.

Benedict's Solution. Benedict has modified Fehling's solution and devised a single test solution that does not deteriorate on standing. For qualitative work this solution may be prepared as follows: Dissolve 20 g. of sodium citrate and 11.5 g. of anhydrous sodium carbonate in 100 cc. of hot water in a 400-cc. beaker. Add slowly to the citrate-carbonate solution, with continual stirring, a solution of 2 g. of copper sulfate crystals in 20 cc. of water. The mixed solution should be perfectly clear (if not, pour it through a fluted filter).

QUESTIONS

1. What is the precipitate which forms? Compare this result with that obtained in a previous experiment (Experiment 22b).

2. What is meant by the term aldohexose? ketopentose?

3. Of what value is Fehling's test in classifying an unknown sugar?

(B) **Osazone Test.** *Phenylglucosazone.* Place 10 cc. of the glucose solution in a large test-tube, add 6 cc. of *freshly prepared* phenylhydrazine reagent, and 2–3 drops of saturated sodium bisulfite solution (to avoid oxidation). Mix thoroughly, stopper the tube with a wad of cotton, and heat in a beaker of boiling water. Note the time of immersion and record the time at which the osazone [1] precipitates. Shake the tube from time to time to avoid forming a supersaturated solution of the osazone. In applying the osazone test for comparison of various sugars, it is advisable to perform all of the tests simultaneously.

Continue the heating in the bath of boiling water for fifteen or twenty minutes, allow to cool slowly, transfer some of the wet crystals to a microscope slide, and examine under the microscope (compare with Fig. 21). Filter the remainder of the crystals at once with suction and wash with a little water. Allow to dry and take the melting-point (note that osazones discolor on standing).

Preparation of Phenylhydrazine Reagent. Dissolve 4 g. of phenylhydrazine hydrochloride [2] (C_6H_5—NH—NH_2,HCl) in 36 cc. of water and add 6 g. of sodium acetate crystals and a drop of glacial acetic acid. If the resulting solution is turbid, add a *small pinch* of decolorizing charcoal, shake vigorously, and filter the solution. The reagent deteriorates rapidly.

QUESTIONS

1. Compare the melting-points and rates of precipitation of the osazones of the more common sugars, and explain how these values might be used in the identification of an unknown sugar.[3]

2. Explain the fact that glucose and fructose give the *same* osazone:

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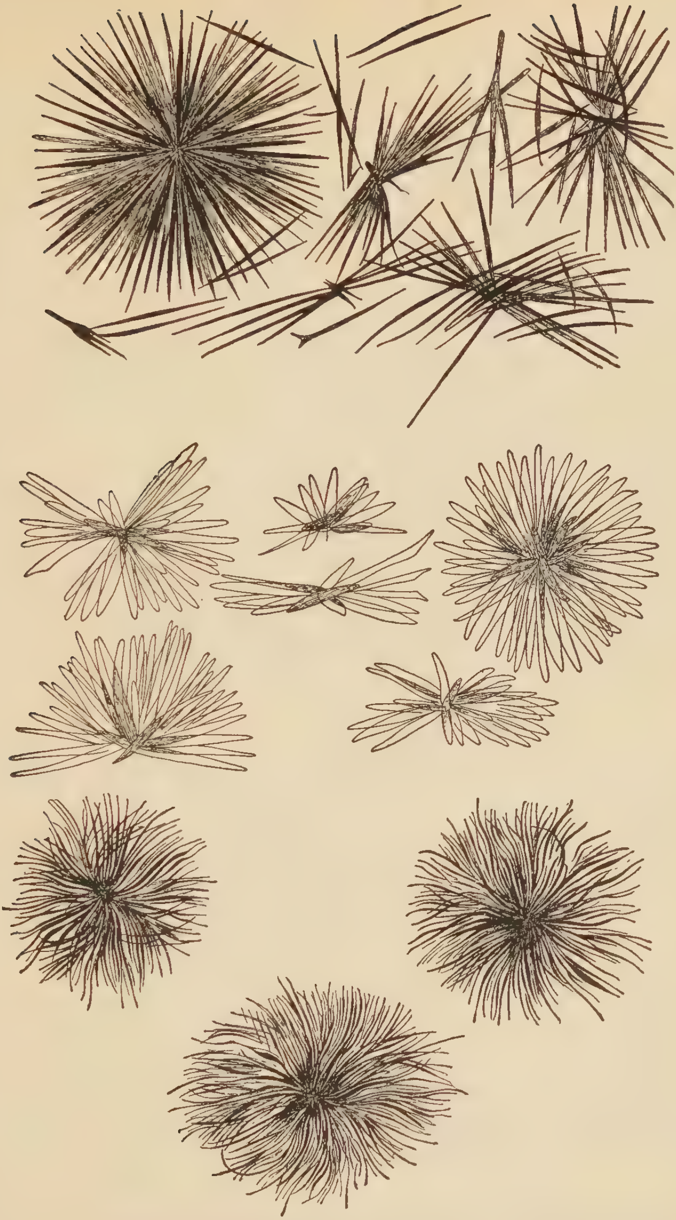
[1] A few sugars yield sparingly soluble phenylhydrazones, so that the precipitate obtained at first is not the osazone but the phenylhydrazone, *e.g.*, *d*-mannose.

[2] A satisfactory reagent may also be made by dissolving 4 g. (4 cc.) of phenylhydrazine (the free base is a liquid) in a solution of 4 g. (4 cc.) of glacial acetic acid in 36 cc. of water, and clarifying as above with a pinch of decolorizing charcoal. This procedure is less desirable owing to the poisonous character of phenylhydrazine (vapor or liquid). If the liquid comes in contact with the skin it must be washed off at once, using 5 per cent acetic acid, followed by soap and water.

[3] Consult Mulliken, *The Identification of Pure Organic Compounds*, Vol. 1, pages 28–38; Kamm, *Qualitative Organic Analysis*, second edition, page 175; Clarke, *Handbook of Organic Analysis*, pages 161–165; Shriner and Fuson, *The Systematic Identification of Organic Compounds*, second edition, page 64.



Upper form, dextrosazone; central form, maltosazone; lower form, lactosazone. Copied from Hawk, *Practical Physiological Chemistry*, P. Blakiston's Son & Co.

FIG. 21.—Crystals of Osazones.

(C) **Acetylation of Glucose.** In a porcelain mortar, finely pulverize 6 g. of dry glucose and mix thoroughly with 3 g. of fused sodium acetate. Transfer the mixture to a 200-cc. round-bottom flask and add 30 g. (28 cc.) of pure acetic anhydride. Heat the mixture on a steam-bath and agitate vigorously to aid in dissolving the solids (about thirty minutes is required to obtain a clear solution). Heat for two hours longer and pour the warm solution in a thin stream, with vigorous stirring, into 250 cc. of ice-cold water in a beaker. Disintegrate any lumps of the crystalline precipitate and allow the finely divided material to stand in contact with the water, with occasional stirring, until the excess acetic anhydride has been hydrolyzed. This will require about two hours. Filter the crystals with suction and press as dry as possible with a clean cork or porcelain spatula. Transfer the crystals to a beaker, mix thoroughly with about 250 cc. of water, and allow to stand with occasional stirring, for about two hours longer. Filter the crystals with suction and press as dry as possible on the filter. Recrystallize the crude β-glucose penta-acetate from about 25 cc. of ordinary ethyl alcohol. The yield of purified β-glucose penta-acetate is 7–8 g. Determine the melting-point of the purified material.

QUESTIONS

1. What is the significance of the fact that five acetyl groups can be introduced into the molecule of glucose or fructose?
2. What is the significance of the fact that only eight acetyl groups (and not ten) can be introduced into the molecule of the disaccharide, sucrose (which yields one molecule of glucose and one molecule of fructose upon hydrolysis)?
3. Give an accurate definition of the term carbohydrate.

Fructose (*d*-Fructose, Fruit Sugar, Levulose) $C_6H_{12}O_6$. Prepare a solution of 1 g. of pure fructose in 50 cc. of distilled water and use this solution in carrying out the tests given in paragraphs (A) and (B) under glucose.

If any of the following monosaccharides are available, they may be tested as for glucose and fructose: *d*-Galactose (an aldohexose), *d*-Mannose (an aldohexose), *d*-Xylose (an aldopentose), *l*-Arabinose (an aldopentose).

(b) Disaccharides

Sucrose (Cane Sugar, Beet Sugar, Saccharose) $C_{12}H_{22}O_{11}$. Prepare a solution of 1 g. of sucrose in 50 cc. of distilled water and use this solution in carrying out the tests given in paragraphs (A) and (B) under glucose.

(C) **α-Naphthol Reaction (Molisch's Test).** To about 5 cc. of the sucrose solution add 2 drops of a 15 per cent solution of α-naphthol in 95 per cent ethyl alcohol (Molisch's reagent). In another test-tube place about 5 cc. of concd. sulfuric acid, incline the tube at a 45° angle, and cautiously pour the sugar solution down the inside of the tube so that it floats on the surface of the acid without mixing. Observe the color at the junction of the liquids. Compare with a control experiment using 5 cc. of water + 2 drops of Molisch's reagent.

This color reaction is due presumably to the formation of a furan derivative (furfural, hydroxymethylfurfural, etc.) which reacts with α-naphthol to give a highly colored condensation product. This test is given by all substances containing a carbohydrate group (glycosides, glycoproteins, nucleic acids, etc.), consequently it has little value except to detect the presence of carbohydrates. The Molisch test must not be confused with the furfural reaction, which is specific for pentoses, methylpentoses, and pentosans. The latter group yield furfural (or methylfurfural) by distillation with 12 per cent hydrochloric acid, and the furfural is detected (or determined quantitively) *in the distillate* by combination with phloroglucinol, etc.

(D) **Hydrolysis.** To the remainder of the solution, add 1–2 cc. of dil. hydrochloric acid and heat on a steam-bath for half an hour. Carefully *neutralize* with dil. sodium hydroxide solution (10 per cent) and again apply Fehling's test for reducing sugars.

Lactose (Milk Sugar) $C_{12}H_{22}O_{11} + H_2O$. Prepare a solution of 1 g. of pure lactose in 50 cc. of water and use this solution in carrying out the tests given in paragraphs (A) and (B) under glucose, and (C) and (D) under sucrose.

Maltose (Malt Sugar) $C_{12}H_{22}O_{11} + H_2O$. Prepare a solution of 1 g. of maltose in 50 cc. of water and carry out tests (A) and (B) under glucose, and (C) and (D) under sucrose.

Carbohydrates are divided generally into three classes: monosaccharides, disaccharides, and polysaccharides. The monosaccharides are polyhydroxyaldehydes or polyhydroxyketones. The disaccharides are built up from two monosaccharide molecules with elimination of one molecule of water, the polysaccharides from many monosaccharide molecules with loss of a molecule of water for each monosaccharide unit. Thus, a six-carbon monosaccharide has the formula $C_6H_{12}O_6$, the corresponding disaccharide, the formula $C_{12}H_{22}O_{11}$ and the corresponding polysaccharide, the formula $(C_6H_{10}O_5)_n$.

As monosaccharides contain several hydroxyl groups as well as an aldehyde or ketone group, it might be anticipated they would form intramolecular acetals. Acetals, in general, are produced from an alcohol and an aldehyde in the presence of an acid catalyst, by a stepwise process involving the hemi-acetal as an intermediate stage:

$$\text{RCHO} + \text{R'OH} \overset{\text{HX}}{\rightleftarrows} \underset{\text{hemi-acetal}}{\text{RCHOH(OR')}} + \text{R'OH} \overset{\text{HX}}{\rightleftarrows} \underset{\text{acetal}}{\text{RCH(OR')}_2} + H_2O$$

Investigations have shown that monosaccharides (either aldoses or ketoses) exist in solution in an equilibrium involving the open-chain hydroxyaldehyde or hydroxyketone structure and two stereoisomeric cyclic forms of hemi-acetal type (α- and β-forms). The latter can be isolated in the form of stable derivatives, such as α- and β-glucose penta-acetates, α- and β-methyl glucosides, etc., when monosaccharides are subjected to acylation or alkylation.

Disaccharides are formed from two monosaccharide molecules either by acetal-like linkage between the two aldehyde and ketone groups, or by linkage between the aldehyde or ketone group of one monosaccharide molecule and an alcohol group of the second monosaccharide. If the aldehyde (or ketone) groups of both monosaccharide units are used in the linkage, the resulting disaccharide will not have reducing action (trehalose type); if only one aldehyde (or ketone) group is used in linking the two units, then the resulting disaccharide will have reducing action toward Fehling's solution (maltose type). Owing to the fact two functional groups are used in holding the monosaccharides units in combination, disaccharides such as sucrose and maltose yield octa-acetates and not deca-acetates upon acetylation.

QUESTIONS

1. What sugars are present in the solution after hydrolysis of sucrose? Will these sugars form an osazone with phenylhydrazine?
2. Why is the hydrolysis of sucrose sometimes referred to as the inversion of sucrose? What is invert sugar?
3. What other agents besides acids promote the hydrolysis of complex carbohydrates?

Experiment 27

CARBOHYDRATES—STARCHES

Polysaccharides $(C_6H_{10}O_5)_n$

Preparation of Potato Starch. Peel a medium-sized raw potato, record the weight, and grate the potato into a very fine pulp through a grater. Mix the pulp with about 500 cc. of water, shake vigorously in a large flask, and strain the mixture through cheese-cloth to remove the coarse particles. Allow the strained starch suspension to settle, and wash the starch by decantation with several portions of water. Allow the compact mass to drain as completely as possible, and spread it on a large watch glass to dry in the air. Weigh the dried starch and compare with the weight of the potato. If desired, this starch may be used for the following tests.

Behavior of Starch. Prepare a colloidal starch solution in the following way. Mix 1 g. of starch with 15 cc. of cold water and stir in a mortar until a uniform suspension, free from lumps, is obtained. Pour this suspension slowly with stirring into 135 cc. of boiling water and continue to boil for a few minutes after all of the starch has been added. Use this colloidal starch solution for the following tests.

(A) **Iodine Test.** To 1 cc. of the colloidal starch solution add 9 cc. of water and mix thoroughly. To this diluted solution add 10 cc. of water containing *2 drops* of iodine solution (prepared by dissolving 10 g. of iodine crystals in a solution of 20 g. of potassium iodide in 80 cc. of water). The resulting solution contains approximately one part of starch in three thousand parts of the solution.

Dilute this solution decimally (by adding 1 cc. of the solution to 9 cc. of water, and continuing this process) until the blue color becomes very faint. Calculate roughly how small a concentration of starch, in parts per million, will give a perceptible test with iodine solution.

(B) **Fehling's Test for Reducing Sugars** (see Exp. 26, page 195). Perform this test with 3–4 cc. of the colloidal starch solution. Explain the result.

(C) **α-Naphthol Reaction (Molisch's Test).** To about 5 cc. of the colloidal starch solution add 2 drops of a 15 per cent solution of α-naphthol in 95 per cent ethyl alcohol (Molisch's reagent). In another test-tube place about 5 cc. of concd. sulfuric acid, incline the tube at a 45° angle, and cautiously pour the starch solution down the inside of the tube so that it floats on the surface of the acid without mixing. Observe the color at the junction of the liquids.

This color reaction is due presumably to the formation of a furan derivative (furfural, hydroxymethylfurfural, etc.) which reacts with α-naphthol to give a highly colored condensation product. This test is given by all substances containing a carbohydrate group (glycosides, glycoproteins, nucleic acids, etc.), consequently it has little value except to detect the presence of carbohydrates. The Molisch test must not be confused with the furfural reaction, which is specific for pentoses, methylpentoses, and pentosans. The latter group yield furfural (or methylfurfural) by distillation within 12 per cent hydrochloric acid, and the furfural is detected (or determined quantitatively) *in the distillate* by combination with phloroglucinol, etc.

(D) **Hydrolysis by Acids.** To 50 cc. of the colloidal starch solution add 4–5 drops of concd. hydrochloric acid and heat on a steam-bath for thirty to forty minutes. Cool to room temperature and *neutralize* with dil. sodium hydroxide solution (10 per cent). Now perform Fehling's test for reducing sugars, and the iodine test. Explain the results.

(E) **Hydrolysis by Enzymes.** To 50 cc. of the colloidal starch solution in a clean flask, add 1–2 cc. of saliva and mix well. Place the flask in a bath of water maintained at 38–40° and allow to remain for twenty minutes or longer. Perform Fehling's test for reducing sugars, and the iodine test. Explain the results.

QUESTIONS

1. Where are starches most commonly found?
2. What are the following substances: dextrin? inulin? glycogen? gum arabic?
3. Explain briefly the metabolism of starches in the human body. Name the enzymes involved in the digestion of starches.

Experiment 28

CARBOHYDRATES—CELLULOSE

Polysaccharides $(C_6H_{10}O_5)_m$

Cellulose. This complex polysaccharide forms a large portion of the cell walls and supporting framework of plants. It is insoluble in most of the common solvents, and is more complex than the starches and not so readily hydrolyzed. Absorbent cotton and washed filter paper are almost pure cellulose, and are used in the following tests as typical examples of cellulose. Wood contains in addition to cellulose a substance called lignin, which is probably combined in the form of a lignocellulose. Recent work indicates that the fundamental cellulose in all plants is the same chemical individual.

(A) **Parchment Paper.** Dip a 3-cm. strip of filter paper into a cold solution of sulfuric acid (two vols. of concd. acid to one vol. of water) and after exactly fifteen seconds transfer the paper to a beaker filled with cold water. Wash thoroughly with water, then with very dil. aqueous ammonia. Wash out all of the ammonia with pure water and allow to dry. Parchment paper is formed in this way.

(B) **Hydrolysis.** In a mortar, triturate a shredded washed filter paper or a wad of absorbent cotton, with 2–3 cc. of concd. sulfuric acid. Cautiously add 50 cc. of water, transfer to a beaker, and boil gently for thirty minutes. Keep the volume of the solution constant by adding water from time to time as the solution evaporates. Cool the solution and *neutralize* carefully with strong sodium hydroxide solution (20 per cent). Apply Fehling's test for reducing sugars (see Exp. 26, page 195).

(C) **Acetylation.** *Cellulose Acetate.* In a small beaker place 20 g. (20 cc.) of glacial acetic acid, 6 g. (6 cc.) of acetic anhydride, and *2 drops* of concd. sulfuric acid (from a glass rod). Introduce 0.5 g. of absorbent cotton into the solution and cover the beaker with a watch glass. From time to time press the cotton into the solution, in order to remove the bubbles which it retains and which

tend to make it rise out of the solution. Allow to stand for at least twenty-four hours.

Pour the clear solution in a thin stream with vigorous stirring, into about 500 cc. of water in a large beaker. Filter the gelatinous precipitate with suction on a large Büchner funnel, and squeeze the crude cellulose acetate in a cotton cloth to remove the water as completely as possible. Allow the material to dry in the air.

In a test-tube treat about one-fourth of the perfectly dry cellulose acetate with 5 cc. of chloroform. The material will dissolve slowly. Pour the solution onto a watch glass and allow the solvent to evaporate gradually. Pour water onto the film and allow to stand for a few minutes. Carefully remove the film from the glass, allow to dry, and test its inflammability by touching the edge with a lighted match, held in a pair of tongs. Test the solubility of the remainder of the cellulose acetate in ethyl alcohol, ether, and ethyl acetate.

(D) **Cellulose Nitrates.** *Pyroxylin* (*collodion-cotton*). In a 250-cc. beaker mix *carefully*, exactly 10 cc. of water, 68 cc. of concd. sulfuric acid, and 30 cc. of concd. nitric acid. Cool the solution to 30° and introduce 1 g. of absorbent cotton, in a single piece. Stir the mixture from time to time and maintain at a temperature of 30° for twenty minutes. At the end of this time remove the nitrated cotton by means of a glass rod and transfer immediately to a large volume of cold water. Wash thoroughly with cold water, and finally with warm water, until the washings do not show an acid reaction to litmus paper. Squeeze as dry as possible and spread out to dry in the air, at *room temperature*. The product obtained in this way contains about 11.0 per cent nitrogen. It is a mixture of the lower nitrates, with only a small quantity of the trinitrate (mono-nitrate = 6.77 per cent nitrogen, di-nitrate = 11.13 per cent nitrogen, tri-nitrate = 14.17 per cent nitrogen).

Hold a small piece of the dry pyroxylin by means of tongs and touch it to a flame.

Treat the remainder of the dry pyroxylin with a mixture of 10 cc. of ether and 10 cc. of absolute ethyl alcohol. Allow to stand overnight in a corked test-tube and decant the clear solution; this is collodion. Pour some of this solution onto a watch glass and allow the solvent to evaporate slowly. Pour water onto the film and allow to stand for a few minutes. Carefully remove the film from the

glass, allow to dry, and test its inflammability by touching the edge with a lighted match, held in a pair of tongs. Compare with the film of cellulose acetate.

Pour the residual collodion solution into a bottle provided for this purpose on the side-shelf.

Cellulose is insoluble as such in all solvents. However, it will form soluble or colloidal complexes in certain heavy metal salt solutions, such as zinc chloride in concentrated hydrochloric acid, cuprammonium nitrate, etc. When precipitated from these solutions by dilution or other means, a partially hydrated cellulose is obtained which in the fiber form is known as rayon. Another very commonly used method for producing rayon is known as the viscose process. This consists in treating cellulose with sodium hydroxide and carbon disulfide to give a cellulose xanthogenate ("xanthate") in which the cellulose hydroxyls have been converted to —O—CS—SNa groups. This product forms a viscous colloidal solution in water and upon acidification the xanthate groups are decomposed and a hydrated cellulose is formed, which is rayon. This regenerated cellulose when pressed between rollers gives a transparent sheet known as cellophane. Cellophane sheets are rendered moisture-proof by coating them on both sides with a very thin film of material of which the two most important constituents are paraffin wax and cellulose nitrate.

Cellulose acetate in the form of a fiber is known as celanese and in the form of strips is used for moving picture films or for wrapping material like cellophane. Cellulose acetate is also used as a plastic material. Recently it has been found that on hydrolysis of cellulose acetate, a cellulose is regenerated which may be used in fabrics and resembles rayon but which has a much higher wet strength. Mixed esters of cellulose such as a part propionate and part acetate have been marketed recently.

Newspaper, writing paper, wrapping papers, and paper towels all consist primarily of cellulose (generally from wood) and the difference between them consists for the most part in the degree of refinement of the cellulose and the particular chemical treatment used.

QUESTIONS

1. To what class of organic compounds do cellulose acetate and cellulose nitrate belong? Explain why the term "nitrocellulose" is not scientifically a correct name for cellulose nitrate.

2. Explain briefly the preparation and use of: celluloid; viscose; rayon; mercerized cotton; Schweitzer's reagent.

3. Explain the meaning of the following terms: pentosan; hexosan; galactan; the furfural test.

Experiment 29a

UREA NITRATE AND UREA

From Urine

Urea Nitrate. Under a hood, evaporate in a porcelain dish 500 cc. of fresh urine,[1] first by heating on an asbestos-centered wire-gauze over a burner (until the volume is reduced to about 150 cc.) and *finally by heating on a steam-bath* until a thick syrup remains. Treat the syrup and solid residue with 100 cc. of ethyl alcohol (95 per cent, by volume) and stir the mixture thoroughly. Warm on a steam-bath and stir well to obtain a good extraction. Decant the hot alcohol through a fluted filter paper into a porcelain dish, and repeat the extraction as before with two additional 50-cc. portions of ethyl alcohol. To the alcoholic extracts add 50 cc. of water and concentrate on a steam-bath to a volume of 25–30 cc. Cool in an ice-salt mixture and while stirring thoroughly add drop by drop, from a separatory funnel, pure concd. nitric acid (sp. g. 1.42) until the precipitate of urea nitrate ceases to increase in amount. Usually about 25 cc. of nitric acid is required. During the addition of the nitric acid it is very important to keep the mixture well stirred and thoroughly cooled.

Filter the precipitated urea nitrate with suction (preferably with a hardened filter paper), wash with a small amount of ice-cold concd. nitric acid, and press as dry as possible with a clean cork or porcelain spatula. Dissolve the crude urea nitrate in about 85 cc. of boiling water and add *5–10 drops* of dil. potassium permanganate solution (0.5 per cent). Cool slightly, add 4–5 g. of decolorizing charcoal (Norite), and boil the solution gently for about twenty minutes. Keep the volume constant by adding a small amount of water from time to time as evaporation occurs. Filter the hot solution through a fluted filter and evaporate the filtrate on a steam-bath, to a volume of about 25 cc. Cool in an ice-bath, stir thor-

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[1] The urine should be preserved from decomposition by adding about 10 cc. of toluene if the isolation of urea nitrate is not to be started within a few hours from the time the urine is collected. If toluene is used, it must be separated before evaporating over a burner. If the entire evaporation is effected on a steam-bath, the toluene need not be removed.

oughly, and add drop by drop about 15–20 cc. of concd. nitric acid. Filter the precipitated urea nitrate with suction (preferably with a hardened filter paper) and press as dry as possible with a clean cork or porcelain spatula. Wash the crystals with a small amount of ice-cold concd. nitric acid. The resulting crystals of urea nitrate should be practically colorless; if a colored product is obtained, the purification should be repeated. The yield is 6–10 g. of the dried crystals.

Urea. Weigh the crystals of purified urea nitrate and in a small beaker treat with 15 cc. of distilled water. Then add powdered barium carbonate in small portions, with stirring; for each gram of urea nitrate use 1.2 g. of barium carbonate, which is an excess of 50 per cent over the calculated amount necessary to liberate the urea from the nitrate. It is essential to use an excess of barium carbonate or the urea will be decomposed on warming.

After the evolution of carbon dioxide has ceased, add about 1 g. of decolorizing charcoal (Norite) and heat on the steam-bath for about fifteen minutes. Filter the hot solution through a small fluted filter and wash the charcoal with a few cc. of hot water. Transfer the filtrate (which should be clear and practically colorless) to a small porcelain dish and evaporate nearly to dryness on a steam-bath. During the evaporation crystals of barium nitrate usually separate. Extract the residue without removing the crystals, with two 10-cc. portions of hot ethyl alcohol (95 per cent by volume). Evaporate the alcoholic solution of urea on a steam-bath until crystals begin to separate, allow the solution to cool and to stand for some time in a cool place to obtain a good separation of the urea. Filter the crystals of urea from the cold solution on a small suction filter, and allow to dry in the air. The product should be colorless; if necessary recrystallize from a small quantity of hot ethyl alcohol with the addition of about 0.2 g. of decolorizing charcoal. The yield is 4–6 g.

Carry out the *Reactions of Urea* (page 223) and turn in the remainder of the product.

Answer the questions given under Experiment 29b.

Experiment 29b

WÖHLER'S SYNTHESIS OF UREA[1]

Dissolve 12.5 g. of sodium hydroxide and 12.5 g. of sodium cyanide (*handle with great care*) in 200 cc. of water in a 500–600-cc. beaker. Over a period of about twenty minutes add 26.8 g. of *finely pulverized* potassium permanganate, in small portions with stirring. The temperature of the solution must not be allowed to rise above 60°. After all of the permanganate has been added, place the beaker in a water-bath and heat at 55–60° for two hours with frequent stirring. Destroy any unreacted permanganate by adding a solution of 1 g. of sodium bisulfite in 4–5 cc. of water. Filter the colorless solution through a Büchner funnel and wash the manganese dioxide with three 10-cc. portions of water. (What compounds are present in the filtrate?)

Place the filtrate containing the sodium cyanate [1] in a 600-cc. beaker, add 50 g. of ammonium sulfate, and evaporate the resulting solution (preferably in a hood) over a burner to a volume of 100–120 cc. Transfer the solution to an evaporating dish and evaporate to dryness on a steam-bath. Stir the material frequently in this process.

Powder the dry solid residue and transfer to a 250–300-cc. beaker. Add 30 cc. of methyl alcohol, heat to boiling on a steam-bath, and filter the mixture rapidly on a Büchner funnel. Return the solid material to the beaker and extract again with 30 cc. of boiling methyl alcohol. Finally, wash the residue on the filter with 10 cc. of boiling methyl alcohol. Combine the filtrates and chill *thoroughly* in a ice-salt mixture. Filter the crystals of urea rapidly, with suction, and allow to dry in the air. The yield is 6–6.5 g. A small additional quantity of urea can be obtained by re-extracting the solid residue with the mother-liquor from which the urea was separated.

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[1] If potassium *cyanate* (KCNO) is available, this experiment can be shortened by omitting the preparation of sodium cyanate. In this case, 20 g. of potassium cyanate is dissolved in 100 cc. of distilled water and 25 g. of ammonium sulfate is added. The filtered solution is evaporated to dryness, and the urea extracted as described above.

Reactions of Urea

(A) Dissolve 0.2 g. of urea in 5 cc. of water, add 5–10 cc. of a solution of sodium hypochlorite or sodium hypobromite.[1]

(B) Dissolve 0.2 g. of urea in 5 cc. of water, add *one drop* of concd. hydrochloric acid and a small crystal of sodium nitrite.

(C) Dissolve 0.2 g. of urea in 5 cc. of cold sodium hydroxide solution (10 per cent) and test the odor of the solution. Heat to boiling and again test the odor. Hold a strip of moist red litmus paper *in the vapor*.

(D) Dissolve 0.2 g. of urea in a few drops of water, add 1 cc. of concd. nitric acid, and cool. What is the precipitate?

(E) In a test-tube heat gently 0.1 g. of urea until melted and warm gently for two minutes so that bubbles are produced in the liquid. Cool and add 10 cc. of water. Add one drop of very dilute copper sulfate solution and one drop of dil. sodium hydroxide solution (10 per cent). What is formed on heating urea?

QUESTIONS

1. What is the source of the nitrogen which is eliminated from the body in the form of urea?
2. What special significance is attached to the synthesis of urea from ammonium cyanate, which was effected by Wöhler in 1828?
3. Outline by means of equations, a modern commercial method for the preparation of urea starting from coke (carbon).
4. To what general class of organic compounds does urea belong? To what particular acid is urea related?
5. What is biuret? What important class of compounds (occurring in nature) give the biuret reaction?

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[1] Prepared by treating 5–10 cc. of bromine water with sodium hydroxide solution (10 per cent), drop by drop, until the bromine color is just discharged.

Experiment 30

BROMOBENZENE AND *p*-DIBROMOBENZENE

Fit a 500-cc. round-bottom flask with a two-hole cork which holds a short reflux condenser and a small separatory funnel having a *tightly fitting* stopcock. Provide the upper end of the reflux condenser with a one-hole cork holding a delivery tube bent twice at right angles to form a U. Connect this by means of a short rubber tube to a 50–60 mm. funnel inverted over 250–300 cc. of water in a large beaker (see Fig. 18, page 139). This arrangement is made to absorb the hydrogen bromide formed during the bromination. Often small amounts of benzene and bromine are carried over with the hydrogen bromide.

In the 500-cc. flask place 33 g. (40 cc.) of benzene and as a halogen carrier add 2–3 g. of iron in the form of wire or tacks (or 0.5 g. of anhydrous aluminum chloride). *Carefully* pour 60 g. (19 cc.) of bromine through a small funnel, into the separatory funnel. Allow 1–2 cc. of bromine to flow into the benzene, and if necessary warm the flask slightly to start the reaction. When the evolution of hydrogen bromide has started, drop in slowly the remainder of the bromine, so that the reaction proceeds quietly. The addition of the bromine should be carried out over a period of about an hour. After all of the bromine has been added, warm the mixture slightly until no red vapors are visible above the liquid.

➔**Caution:** Be very careful in handling bromine, since the liquid produces painful burns and the vapors are obnoxious. Watch carefully to avoid leakage of bromine around the stopcock of the separatory funnel. The best treatment for bromine burns is the application of a liberal quantity of glycerol immediately. Follow the glycerol treatment by a thorough washing with water, dry the skin and apply a healing ointment or salve.

Wash the product several times with water, then steam distil by passing steam into the mixture and attaching a good water-cooled condenser. A partial separation of bromobenzene and *p*-dibromobenzene is made during the steam distillation. Collect the first portion of the distillate until crystals of *p*-dibromobenzene

separate in the condenser tube, then change the receiver and collect the second portion, until all of the *p*-dibromobenzene has passed over. Reject the material which does not steam distil.

➔**Caution:** During the steam distillation, when *p*-dibromobenzene starts to solidify in the condenser, watch carefully to avoid the formation of a crystalline mass which will completely obstruct the tube. If a solid mass collects in the tube, stop the flow of water through the condenser *momentarily* and drain the water from the condenser jacket. The heat from the vapors will then melt the crystals and the obstruction will be removed. As soon as this occurs, start the water again in the condenser jacket.

Bromobenzene. From the first portion of the steam distillate separate the heavy liquid, which is chiefly bromobenzene. Dry with 3–4 g. of anhydrous calcium chloride and distil on an asbestos-centered wire-gauze, using an air-cooled condenser. Reject any material which distils below 140°, and collect for redistillation the fraction boiling at 140–170°. Pour the residue in the distilling flask, while it is still hot, into a small beaker or a watch glass and save for the isolation of *p*-dibromobenzene. Redistil the 140–170° fraction and collect as bromobenzene, the portion boiling at 150–160°. If an appreciable residue remains in the flask save this for isolation of *p*-dibromobenzene. The yield of bromobenzene is about 30 g.

***p*-Dibromobenzene.** Filter the second portion of the steam distillate with suction and press the crystals as dry as possible. Combine these crystals with the residue from the distillation of the bromobenzene, and crystallize from hot alcohol with the addition of 1–2 g. of decolorizing charcoal. Use about 4 cc. of alcohol for 1 g. of material to be crystallized. Filter the hot solution through a fluted filter, cool the filtrate thoroughly, and filter the crystals with suction. The yield of *p*-dibromobenzene is about 5–10 g.

In this experiment calculate two theoretical yields by assuming a complete reaction to form: (a) bromobenzene; (b) *p*-dibromobenzene. Calculate the percentage yield of each product, and obtain the total percentage yield by taking the sum of the two.

QUESTIONS

1. Illustrate by means of equations, *addition* and *substitution* of bromine.
2. Indicate what substances would be formed by the action of bromine on the following compounds: benzoic acid; nitrobenzene; chlorobenzene; naphthalene; toluene—in the presence of iron and absence of sunlight; toluene—at the boiling-point in the presence of sunlight.

Experiment 31a

SODIUM BENZENESULFONATE

In a 200-cc. round-bottom flask, place 85 g. (45 cc.) of fuming sulfuric acid (sp. g. 1.88), containing about 7 per cent of sulfur trioxide, and add with shaking 20 g. (23 cc.) of benzene, a few cc. at a time. Wait until the first portion of benzene has reacted (and dissolved) before adding the next portion. Keep the temperature of the reaction mixture above 30° and below 50°, by occasional cooling in a dish of cold water. When the benzene has dissolved completely, cool, and pour the solution slowly with stirring into about 200 cc. of water. Cool to room temperature and if necessary filter from any diphenylsulfone, ($C_6H_5—SO_2—C_6H_5$), which may separate. Partly neutralize the excess sulfuric acid by adding *carefully* 25 g. of solid sodium bicarbonate; then add 50 g. of clean salt (sodium chloride) and warm until it dissolves. Filter the hot solution with suction through a previously warmed Büchner funnel, transfer the warm filtrate to a beaker, and cool rapidly with stirring. Allow the mixture to stand for about an hour, in an ice-bath, with occasional stirring.

When the sodium benzenesulfonate has separated completely, filter with suction and press the crystals as dry as possible with a porcelain spatula or a clean cork. Moisten with 30–40 cc. of a filtered, saturated salt solution, and again filter with suction and press as dry as possible. Allow the sulfonate to dry by spreading it on a porous clay plate. If the product is washed with a little ordinary alcohol it will dry more rapidly. The yield is 20–25 g. of the dry sodium salt. The product contains traces of sodium chloride and other salts but is pure enough for most laboratory purposes. These impurities can be completely removed by crystallization from hot ethyl alcohol (95 per cent). About 15–18 cc. of alcohol is necessary for each gram of sodium benzenesulfonate to be crystallized. Do not attempt to determine its melting-point.

Answer the questions given under Experiment 31c.

Experiment 31b

SODIUM *p*-BROMOBENZENESULFONATE

In a 200-cc. round-bottom flask, place 35 g. (18 cc.) of fuming sulfuric acid (sp. g. 1.88), containing about 7 per cent of sulfur trioxide, and add 16 g. (11 cc.) of bromobenzene, in small portions and with constant stirring, so that the temperature does not exceed 100°. In case the sulfonation proceeds slowly, warm the flask gently on a steam-bath after all of the bromobenzene has been added, and shake the mixture until all of the bromobenzene has passed into solution. After cooling, pour the solution cautiously into about 65 cc. of water. If a precipitate separates at this point due to the formation of a little dibromodiphenylsulfone, ($BrC_6H_4—SO_2—C_6H_4Br$), filter the warm solution with suction. Add 25 g. of clean salt (sodium chloride) to the filtrate and warm on the steam-bath until the salt dissolves.

Cool the solution rapidly with stirring and the sodium *p*-bromobenzenesulfonate separates. Filter with suction and press the crystals as dry as possible with a porcelain spatula or a clean cork. The product still contains considerable amounts of sodium chloride and sulfuric acid. To effect a partial purification, pulverize thoroughly, transfer to a large beaker, and mix well with a filtered solution of 9–10 g. of sodium chloride in 35–40 cc. of water. Heat on a steam-bath for a short while, cool, filter the product, and press as dry as possible. Allow the salt to dry by spreading it on a porous clay plate. If the product is washed with a little ordinary alcohol it will dry more rapidly. The yield is 20–22 g. of the dry sodium salt. The product contains traces of sodium chloride and other impurities but is pure enough for most laboratory purposes. These impurities can be removed by crystallization from hot ethyl alcohol (95 per cent by volume). About 25 cc. of alcohol is necessary for each gram of sodium *p*-bromobenzenesulfonate to be crystallized. Do not attempt to determine the melting-point of this substance.

Answer the questions given under Experiment 31c.

Experiment 31c

SULFANILIC ACID

In a 200-cc. round-bottom flask, place 14 g. (14 cc.) of freshly distilled aniline and add cautiously in small portions, 40 g. (22 cc.) of concd. sulfuric acid. Attach an air-cooled reflux condenser and heat the flask in an oil-bath at 180–190° for four to five hours. To test for the completion of the reaction add one or two drops of the reaction mixture to 5–6 cc. of dil. sodium hydroxide solution (10 per cent). If a clear solution results, the aniline has been completely sulfonated; if oily drops of unreacted aniline separate, the heating should be continued. In carrying out this test it is essential to use enough sodium hydroxide solution so that the test portion has a strongly alkaline reaction to litmus.

Cool the reaction mixture to room temperature and pour with stirring into about 100 cc. of cold water. The crude sulfanilic acid separates as a gray crystalline mass. Filter with suction, wash with 25–30 cc. of cold water, and crystallize the product from hot water, with the addition of 2–3 g. of decolorizing charcoal. The yield is 12–14 g.

Sulfanilic acid crystallizes from water with two molecules of water of crystallization. Take this into account in calculating the theoretical yield. Anhydrous sulfanilic acid may be obtained by crystallization of the dihydrate from concd. hydrochloric acid, or by heating the dihydrate at 100–110° for a short while.

QUESTIONS

1. Write equations indicating the action of the following reagents on sodium benzenesulfonate: fusion with sodium hydroxide; fusion with sodium cyanide; phosphorus pentachloride.
2. How do you account for the fact that sulfanilic acid does not form a salt with hydrochloric acid?
3. Indicate a series of reactions which may be used to prove that the sulfur atom in an aromatic sulfonic acid is directly attached to a carbon atom of the benzene ring.
4. To what properties of the sulfonic acids do you attribute the fact that many synthetic dyes contain sulfonic acid groups?
5. What products are formed when naphthalene is sulfonated? nitrated?

Experiment 32a

NITROBENZENE

In a 500-cc. round-bottom flask place 23.5 g. (27 cc.) of benzene and add in small portions with vigorous shaking between additions, a cooled mixture of 35 g. (25 cc.) of concd. nitric acid and 55 g. (30 cc.) of concd. sulfuric acid. Cool the flask from time to time in running water so that the temperature does not rise above 50–60°. When all of the acid has been added and the temperature no longer rises on vigorous shaking, attach a water-cooled reflux condenser and heat the flask in a water-bath at 60° for forty minutes with frequent shaking. Cool to room temperature and pour the contents of the flask into about 250 cc. of cold water. Separate the layer of nitrobenzene from the acid solution and wash once with 75–100 cc. of water. Separate carefully from the water, dry with 8–10 g. of anhydrous calcium chloride, and distil on an asbestos-centered wire-gauze, using an air-cooled condenser. Collect in a weighed bottle the portion boiling at 200–206°. The yield is 25–30 g. If a residue remains in the distilling flask it is probably *m*-dinitrobenzene, which is formed when the temperature of nitration is not carefully controlled. Be careful to avoid superheating this residue since it may decompose explosively.

➔ **Caution:** The vapor of nitrobenzene is poisonous and should not be inhaled. The liquid is a powerful skin poison. If the liquid is spilled upon the skin it should be removed by washing with a little alcohol, followed by soap and warm water.

QUESTIONS

1. Why is sulfuric acid used in the above nitration?
2. Why is the temperature of nitration kept below 60° in the above experiment?
3. What is formed by the nitration of naphthalene?
4. Mention several important reactions which are characteristic of aromatic compounds and which differentiate them from aliphatic compounds.
5. What is formed by the reduction of nitrobenzene in the presence of acids?
6. What is the structural formula of picric acid? T.N.T.?

Experiment 32b

p-BROMONITROBENZENE

In a 200-cc. round-bottom flask, place 28 g. (19 cc.) of concd. nitric acid and add carefully 37 g. (20 cc.) of concd. sulfuric acid. Cool the mixture to room temperature and add in 2–3-cc. portions, 16 g. (10.5 cc.) of bromobenzene. During the addition of the bromobenzene, which requires about ten minutes, shake the reaction flask continuously and cool in running water if necessary, to keep the temperature between 50° and 60°. After all of the bromobenzene has been added and the temperature no longer tends to rise from the heat of reaction, place the mixture on a steam-bath and heat for half an hour.

Cool to room temperature and pour the reaction mixture into about 100 cc. of cold water. Filter with suction the crude *p*-bromonitrobenzene (which contains some *o*-bromonitrobenzene), wash with water, and press on the filter with a clean cork or a porcelain spatula. To purify the product crystallize from 100–125-cc. of hot ethyl alcohol. The ortho isomer is more soluble and remains in solution in the alcohol, while the para isomer crystallizes on cooling the solution. The yield of pure *p*-bromonitrobenzene is 10–14 g.

➔ **Caution:** All nitro compounds are poisonous and must be handled carefully. If any nitro compound comes in contact with the skin it should be removed by washing with a little alcohol, followed by soap and water.

QUESTIONS

1. Why is it customary to use concd. sulfuric acid along with concd. nitric acid in nitrations?
2. What position will be taken by the entering nitro group when the following substances are nitrated: phenol? acetanilide? methyl benzoate? nitrobenzene? sulfanilic acid? toluene? benzaldehyde?

Experiment 33a

ETHYL BENZENE

The Friedel-Crafts Reaction

In a dry 500-cc. round-bottom flask attached to a long water-cooled reflux condenser, place 44 g. (33 cc.) of ethyl bromide and 150 g. (170 cc.) of benzene. To provide for the hydrogen chloride and hydrogen bromide evolved during the reaction, fit the top of the condenser with a cork holding a delivery tube bent twice at right angles to form a U. Connect the open end by means of a short rubber tube to a 50–60 mm. funnel inverted [1] over 250–300 cc. of water in a large beaker (see Fig. 18, page 139).

Add 12 g. of pulverized *anhydrous* aluminum chloride and allow the reaction to proceed in the cold, shaking the flask occasionally. When the evolution of halogen acid has slowed down, warm the flask gently on a steam-bath, and finally reflux the mixture on a steam-bath for about an hour. Cool the reaction mixture and pour with stirring into a mixture of 200 g. of ice, 100 g. of water, and 24 g. (20 cc.) of concd. hydrochloric acid. Stir thoroughly to complete the decomposition of any organo-aluminum compounds and transfer to a large separatory funnel. Separate the benzene layer, dry with 10–15 g. of anhydrous calcium chloride, and decant the dried liquid into a 500-cc. round-bottom flask. Fit the flask with a fractionating column and fractionally distil the mixture (see Fractional Distillation, p. 47). It is advantageous to distil very slowly and to use a fractionating column filled with short pieces of glass tubing in order to increase the efficiency and to obtain a good separation. It is desirable to wrap the column with asbestos paper.

Change the fractionating column to a 200-cc. round-bottom flask and carefully refractionate all of the fractions boiling above 85°. Collect the ethyl benzene fraction from 132–138°. In order to obtain most of the ethyl benzene, it is advisable to repeat the fractionation of the fore-runs. The yield is 25–30 g.

Answer the questions following Experiment 33b.

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[1] Another suitable arrangement may be made by connecting the rubber tube to a glass tube supported *above* a surface of water in a suction filtering flask.

Experiment 33b

ACETOPHENONE

The Friedel-Crafts Reaction

Provide a 500-cc. round-bottom flask with a reflux condenser and fit the top of the condenser with a two-hole cork—one opening for a small separatory funnel and the other for a delivery tube connected to a funnel inverted over 200–300 cc. of water in a beaker (see Fig. 18, page 139).

In the flask place 88 g. (100 cc.) of pure anhydrous benzene and add 80 g. of pulverized *anhydrous* aluminum chloride (using precautions to avoid exposure of the latter to atmospheric moisture). Through the separatory funnel at the top of the condenser, add slowly 26 g. (24 cc.) of pure acetic anhydride. This addition should be carried out over a period of one-half hour while the contents of the flask are agitated thoroughly. During this time the reaction mixture heats up and a vigorous evolution of hydrogen chloride takes place.

After all of the acetic anhydride has been added and the reaction has commenced to slacken, heat the reaction mixture for half an hour on a steam-bath. Cool, pour the contents of the flask into a mixture of 150 cc. of concd. hydrochloric acid and 150 g. of ice, and if necessary add a small additional amount of concd. hydrochloric acid to dissolve any basic aluminum salts which are precipitated. Add 25 cc. of ether, shake the mixture thoroughly in a large separatory funnel, and separate the benzene layer. Extract the aqueous portion with 25 cc. of ether and add this to the benzene solution. Wash the benzene solution (including the ether extract) with 50 cc. of sodium hydroxide solution (10 per cent), separate and dry with 15–20 g. of anhydrous calcium chloride. Recover the solvent by distillation from a steam-bath and pour the residual oil into a small distilling flask. Add a few chips of clay plate and distil on an asbestos-centered wire-gauze, using an air-cooled condenser. Since there may be some benzene remaining in the residual oil, care should be taken during the initial heating to avoid igniting the

benzene vapor. Collect the acetophenone boiling at 195–202°. The yield is 18–25 g.

The Friedel-Crafts reaction is essentially a method for the alkylation or acylation of benzene (and other aromatic compounds) in the presence of anhydrous aluminum chloride as catalyst. Alkylation reactions involve the use of alkyl halides or olefins:

$$C_6H_6 + C_2H_5Cl\ (+AlCl_3) \longrightarrow C_6H_5{-}CH_2{-}CH_3 + HCl$$
$$C_6H_6 + CH_2{=}CH_2 + (AlCl_3) \longrightarrow C_6H_5{-}CH_2{-}CH_3$$

It is possible that olefins may be produced as intermediate products when alkyl halides are used; a primary halide such as *n*-butyl chloride gives mainly *sec*-butyl benzene, which product is also formed from the olefins butene-1 or butene-2, and also from *sec*-butyl chloride (under mild conditions). Under vigorous conditions *tert*-butyl derivatives may be formed,

$$\begin{array}{l} C_6H_6 + C_2H_5CH_2CH_2Cl \textit{ or } C_2H_5CHClCH_3 \\ \qquad \textit{or } C_2H_5CH{=}CH_2 \end{array} \xrightarrow{(AlCl_3)} C_2H_5CH(C_6H_5)CH_3$$

owing to the powerful activity of aluminum chloride in promoting molecular rearrangements. The fact that methyl chloride and benzyl chloride ($C_6H_5CH_2Cl$) take part in Friedel-Crafts reactions, although they cannot form olefins, indicates that the olefin is not an *essential* intermediate stage.

Aliphatic and aromatic acid halides react with benzene to give ketones. In these reactions at least one mole of aluminum chloride must be used, since this reagent forms a molecular compound with the ketone produced. Acid anhydrides react very similarly to acid chlorides but on account of the mole of organic acid liberated in the reaction two moles of aluminum chloride are necessary. Anhydrides of dibasic acids

$$C_6H_6 + (C_6H_5CO)_2O + 2AlCl_3 \rightarrow C_6H_5COC_6H_5{,}AlCl_3 + C_6H_5CO_2H{,}AlCl_3$$

give ketonic acids: for example, phthalic anhydride and benzene give *o*-benzoyl benzoic acid, important in the synthesis of anthraquinone, and succinic anhydride and benzene give γ-benzoyl propionic acid.

In place of benzene, certain substituted benzenes may be employed. Alkyl, alkoxyl, or halogenated benzenes readily enter into the Friedel-Crafts reaction while nitro, carboxyl, cyano, sulfonic, and ketonic derivatives of benzene usually fail to react.

QUESTIONS

1. Why is such a large excess of benzene used in this experiment?
2. Write equations for the interaction of the following compounds in the presence of aluminum chloride: benzene (in excess) and 1,2-dichloroethane; benzene (in excess) and carbon tetrachloride; chlorobenzene and acetic anhydride; toluene and phthalic anhydride.
3. Indicate how the following substances can be prepared by the Friedel-Crafts reaction: diphenylmethane; triphenylmethane; *p*-tolualdehyde; *m*-bromobenzophenone; desoxybenzoin (phenyl benzyl ketone).

Experiment 34

p-NITROBENZOIC ACID

Oxidation of a Side-Chain

In a 500-cc. round-bottom flask place 23 g. of *p*-nitrotoluene, and a solution of 68 g. of sodium dichromate crystals ($Na_2Cr_2O_7$, $2H_2O$) in 150 cc. of water. Add 170 g. (92 cc.) of concd. sulfuric acid, with constant shaking and *thorough mixing*, and attach a water-cooled reflux condenser. Heat the reaction mixture carefully until oxidation starts, then remove the flame until the vigorous ebullition subsides. When the mixture has ceased to boil from the heat of reaction, replace the flame under the flask and reflux vigorously for two hours. Cool and pour the reaction mixture into 200–250 cc. of cold water. Filter with suction the precipitate of crude *p*-nitrobenzoic acid, and wash on the filter with about 100 cc. of water.

Grind the precipitate thoroughly in a mortar to break up the lumps, and then transfer it to a 500–600-cc. beaker. Add 100–110 cc. of about 5 per cent sulfuric acid [5.5 g. (3 cc.) of concd. sulfuric acid added to 100 cc. of water], warm on a steam-bath, and stir thoroughly to extract the chromium salts as completely as possible from the *p*-nitrobenzoic acid. Cool, filter with suction, and wash twice with about 50-cc. portions of water. Transfer the crude *p*-nitrobenzoic acid to a beaker, break up any lumps of the material, and treat with 180–200 cc. of 5 per cent sodium hydroxide solution. The *p*-nitrobenzoic acid dissolves, and any unchanged *p*-nitrotoluene remains undissolved; chromium salts will be converted to chromium hydroxide or sodium chromite. Add 3–4 g. of decolorizing charcoal (Norite), warm to 50° with stirring for about five minutes, and filter the alkaline solution with suction. Precipitate the purified acid by pouring the alkaline solution with stirring, *into* 200–220 cc. of about 15 per cent sulfuric acid [37 g. (20 cc.) of concd. sulfuric acid added to 200 cc. of water]. Filter the purified acid with suction, wash thoroughly with cold water, and dry. The yield is 18–20 g. The *p*-nitrobenzoic acid obtained in this way is

sufficiently pure for most purposes. To obtain a product of high purity a small sample may be crystallized from a large volume of hot water, or from glacial acetic acid.

Since the melting-point of *p*-nitrobenzoic acid is fairly high (about 240°), do not attempt to use a bath of cottonseed oil for determining this melting-point. For this purpose a bath of Crisco or of di-*n*-butyl phthalate may be used.

Practically all side-chains with a carbon atom directly attached to the benzene ring may be oxidized to carboxylic acid groups. Thus, the xylenes are oxidized to the corresponding phthalic acids. Two other common reagents for oxidizing side-chains in aromatic compounds are potassium permanganate and potassium ferricyanide.

Phthalic anhydride, a very important intermediate in the preparation of anthraquinone dyes and other chemicals, is prepared by the oxidation of naphthalene. The older procedure consisted in the use of fuming sulfuric acid as the oxidizing agent in the presence of a mercury salt as catalyst. This method has now been supplanted by the direct air oxidation in the presence of vanadium oxide as a catalyst. This latter procedure applied to benzene is a convenient commercial process for the preparation of maleic anhydride.

QUESTIONS

1. What reagents are commonly used for the oxidation of side-chains in the aromatic series?
2. What acid is formed by the oxidation of *p*-cymene (*p*-isopropyl toluene) with excess of potassium permanganate solution?
3. What acid is formed by the oxidation of naphthalene by acidic reagents?
4. What is the technical method of preparing phthalic acid?
5. How may *p*-aminobenzoic acid be prepared from *p*-toluidine?
6. Compare the ease of oxidation of toluene, benzyl alcohol, and benzaldehyde.
7. If you were given a substance which might be either *o*-, or *m*-, or *p*-chlorotoluene (all three of which boil at about the same temperature), how would you identify the substance with certainty?

Experiment 35

ANILINE

In a 500-cc. round-bottom flask provided with an air-cooled reflux condenser, place 25 g. (21 cc.) of nitrobenzene and 45 g. of granulated tin. Shake the mixture thoroughly and add through the condenser tube, in small portions (not exceeding 10 cc. each at the beginning), 120 g. (100 cc.) of concd. hydrochloric acid. The reaction mixture becomes warm and the reaction is controlled by dipping the flask into a dish of cold water, but not cooling enough to prevent the reaction mixture from boiling quietly. When the initial reaction moderates add a second portion of 10 cc. of hydrochloric acid, and continue the addition in this manner. After about half of the total amount of acid has been added increase the portions to about 15 cc. each, using the above precautions. It is necessary to shake the mixture *thoroughly* during the reaction in order to obtain complete reduction. After all of the acid has been added warm the mixture on the steam-bath for thirty minutes.

➤ **Caution:** The reaction mixture must be watched carefully when first placed upon the steam-bath. If it has been kept so cold in the beginning that the reaction was slowed down too much, it will now suddenly become so violent that the contents of the flask may be blown out through the condenser tube.

After this heating it should no longer be possible to detect the odor of nitrobenzene, and a few drops of the reaction mixture should give a perfectly clear solution when poured into water (Why?). During the course of the experiment, especially during cooling, the double salt of aniline hydrochloride and stannous or stannic chloride may separate as a white or yellow crystalline solid.

Cool the reaction mixture to room temperature and add a solution of 75 g. of solid sodium hydroxide in 100 cc. of water, with further cooling if necessary. The reaction mixture must be strongly alkaline at this point, and the aniline separates as an oil. Transfer to a 1-l. round-bottom flask and steam distil[1] the mixture by passing a rapid current of steam into the liquid, and connecting the

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[1] Consult the appendix, "Vapor Pressures of Organic Substances at 100° C."

flask with a good water-cooled condenser. It is desirable to distil the mixture as rapidly as the cooling capacity permits, without loss of product.

Continue the distillation for a short while after the distillate has ceased to be turbid. Saturate the distillate with salt (sodium chloride), using about 25 g. for each 100 cc. of liquid. Transfer to a separatory funnel and extract the aniline with ether, using three successive extractions, with 75 cc. of ether at first, then two portions of 50 cc. each. Dry the combined ethereal solutions in a stout flask or bottle, with crushed *not powdered* solid sodium hydroxide, and shake occasionally during ten to twenty minutes. If an aqueous solution of sodium hydroxide forms at the bottom, separate by decantation and add a fresh quantity of solid sodium hydroxide. Cork the flask and allow to stand for at least twelve hours to complete the drying. Decant from the drying agent into a 500-cc. flask and distil off the ether from a steam-bath; take adequate precautions against fire hazards (see Fig. 19, page 153).

Pour the residual oil into a small distilling flask and distil on an asbestos-centered wire-gauze, using an air-cooled condenser. Since there may be some ether remaining in the aniline, care should be taken during the initial heating to avoid igniting the ether vapor. Collect in a weighed bottle the pure aniline boiling at 180–185°. The yield is 16–18 g.

Tin and hydrochloric acid is a convenient laboratory reagent for reducing nitrobenzene to aniline, but commercially, iron and water with a very small amount of hydrochloric acid is used commonly. The ferrous chloride produced catalyzes the conversion of iron to iron oxide.

Aniline and its derivatives represent a very important group of compounds. Not only are they chemically reactive and therefore lend themselves to further substitution in the benzene ring but the amino group is readily replaced (via the diazotization process) by such groups as hydroxyl, halogen, alkoxyl, cyano, etc. Thus a wide variety of organic compounds may be made from them.

QUESTIONS

1. What is a commercial method of preparing aniline? What procedure is used commercially for isolation of aniline in place of extraction with ether?
2. How could a mixture of aniline and nitrobenzene be separated without using fractional distillation?
3. How are methylaniline and dimethylaniline prepared?
4. Indicate what products would be formed by the action of the following reagents on dimethylaniline: bromine (one mole); ethyl iodide.

Experiment 36

REACTIONS OF PRIMARY, SECONDARY, AND TERTIARY AMINES

Tabulate the results of the following experiments under the headings: (1) Amine used; (2) Solubility in water; (3) Solubility in hydrochloric acid; (4) Solubility in sodium hydroxide solution; (5) Reaction with acetic anhydride; (6) Reaction with benzenesulfonyl chloride; (7) Solubility of benzenesulfonamides in sodium hydroxide solution.

In carrying out many of the following tests only small quantities of the reagents are used. Quantities of reagents must be measured with reasonable care to obtain satisfactory results. It is advantageous to use a small pipette (or simply a glass tube drawn to a small bore at one end). If bottles provided with medicine droppers are available, they are very satisfactory for this purpose.

(A) **General Properties.** Test the solubility of aniline, methylaniline, and dimethylaniline in water, dil. hydrochloric acid, and dil. sodium hydroxide solution, by adding about 2 drops of the amine to be tested to about 5 cc. of the reagent in a test-tube.

(B) **Behavior toward Acetic Anhydride.** Test each of the three amines mentioned above, in the following way. To 1 cc. of the amine in a dry test-tube, add 3 cc. of acetic anhydride, and observe any temperature change. Boil the solution gently over a small flame for three to four minutes, cool slightly, and add cautiously about 10 cc. of cold water. Heat to boiling, then cool rapidly with shaking, and observe the result. If a precipitate is not formed, carefully neutralize with ammonia and observe the result. If a crystalline precipitate forms, filter with suction and wash the crystals with a little water. Crystallize from about 5 cc. of hot water, dry the crystals, and determine the melting-point. Compare the behavior of the three classes of amines toward acetic anhydride and explain.

(C) **Behavior toward Benzenesulfonyl Chloride.** *Hinsberg's Test.* Test each of the three amines mentioned above, in the following way. To 8–10 drops of the amine in a test-tube, add about 8 cc. of dil. sodium hydroxide solution (10 per cent) and 14–15 drops of benzenesulfonyl chloride. Shake thoroughly and observe any reaction. Warm gently with shaking (*do not boil*) until the odor of the benzenesulfonyl chloride can no longer be detected. Cool to room temperature, shake well, and observe. Acidify by adding concd. hydrochloric acid, cool to room temperature, shake well, and observe. If a solid precipitate is formed, filter with suction and wash with water. Crystallize from 3–5 cc. of about 70 per cent alcohol, and determine the melting-point of the crystals. Compare the behavior of the three classes of amines toward benzenesulfonyl chloride and compare the solubilities of the benzenesulfonamides in dil. sodium hydroxide solution.

The arylsulfonyl derivatives of aliphatic and aromatic amines are good crystalline derivatives for identification purposes. If benzenesulfonyl chloride yields a liquid sulfonamide other reagents such as *p*-nitro- or *p*-bromobenzenesulfonyl chloride may be used.

(D) **Formation of a Quaternary Ammonium Compound.** In a dry test-tube, place about 1 cc. of dimethylaniline and add about 2 cc. of methyl iodide. Cork the tube and allow to stand with occasional shaking for about twenty minutes, or until crystals appear. What is this substance?

(E) **Characterization of an Unknown Amine.** Obtain from your instructor a sample of an unknown amine, and apply the tests given above to determine to which class the amine belongs. Report the result on your card for this experiment.

QUESTIONS

1. Write equations showing the action of sodium nitrite and hydrochloric acid upon: aniline; methylaniline; dimethylaniline; methylamine.
2. How would ammonia behave toward benzenesulfonyl chloride in the Hinsberg test?
3. Explain the reactions involved in the carbylamine (isocyanide) test for primary amines.

Experiment 37

ACETANILIDE

In a 200-cc. round-bottom flask fitted with a long air-cooled reflux condenser (60–70 cm. in length), place 20 g. (20 cc.) of aniline and 25 g. (24 cc.) of glacial acetic acid. Boil the mixture gently on an asbestos-centered wire-gauze for five to six hours, and adjust the flame so that the vapors of acetic acid condense about two-thirds of the way up the tube. The water formed in the reaction, along with a *little* acetic acid, should be allowed to escape gradually from the top of the tube, as this will hasten the reaction. It is advisable to place a cork bearing a delivery tube in the top of the condenser, and conduct the water vapor and traces of acetic acid through a short rubber tube to a funnel inverted over 200–300 cc. of water in a beaker.

As the reaction mixture will solidify on cooling, pour it out at once while hot, into a larger beaker containing about 350 cc. of water which is vigorously stirred. Filter the crystalline precipitate and wash with cold water. Recrystallize from hot water with the addition of 1–2 g. of decolorizing charcoal. For filtration use a large fluted filter and a large funnel with a short, wide stem. Cool the filtrate rapidly to obtain small crystals and filter with suction. Wash with a small amount of water and spread the crystals on a clean paper to dry. If the product is dark-colored, repeat the crystallization. The yield of purified acetanilide is 17–20 g.

QUESTIONS

1. What acetylating agents other than glacial acetic acid may be used for the preparation of acetanilide?
2. In the preparation of *p*-nitroaniline, why is aniline converted to acetanilide before nitration?
3. What is the relative toxicity of aniline and acetanilide?
4. What effect do the following reagents have upon acetanilide: hot dil. hydrochloric acid? hot dil. sodium hydroxide solution?

Experiment 38

p-BROMOACETANILIDE

In a 300–400-cc. beaker dissolve 13.5 g. of acetanilide in 50 cc. of glacial acetic acid and add slowly with shaking, 17 g. (5.3 cc. measured from a burette) of bromine. Allow the orange-colored solution to stand at room temperature for about ten minutes to complete the reaction. During this time, especially if the solution is warm, crystals may separate. At the end of this time pour the solution with stirring into 400–500 cc. of distilled water, whereupon the crude *p*-bromoacetanilide precipitates in white or yellow flocks. Rinse the beaker with 15–20 cc. of water. The mixture is sometimes colored with free bromine; the color may be removed by adding a few drops of strong sodium bisulfite solution. Filter the crystalline precipitate with suction, wash thoroughly with cold water, and press as dry as possible on the filter.

To obtain pure *p*-bromoacetanilide crystallize the crude product from hot ethyl alcohol. The yield is 10–15 g.

➔ **Caution:** In measuring bromine from a burette, be very careful to avoid leakage around the stopcock. Treat bromine burns immediately with glycerol, wash thoroughly, dry the skin carefully, and apply an ointment.

QUESTIONS

1. Why are two atoms of bromine used in substituting one atom of bromine into an aromatic compound?
2. Illustrate by equations the difference between *addition* and *substitution* of bromine.
3. What are the two groups, either of which, when present in the benzene ring increases most markedly the ease of further substitution into the ring?
4. How may the ease of further substitution be diminished when either of such groups is present?
5. What substances would be formed by the action of bromine on the following compounds: benzoic acid? nitrobenzene? chlorobenzene? naphthalene? toluene—in the presence of iron as a catalyst and in the absence of sunlight? toluene—at the boiling-point in the presence of sunlight?

Experiment 39

p–BROMOANILINE

Dissolve 10 g. of pure *p*-bromoacetanilide in 20 cc. of boiling ethyl alcohol contained in a 200-cc. round-bottom flask provided with a reflux condenser. Through the condenser tube, add a solution of 5 g. of potassium hydroxide in 6 cc. of water and reflux the reaction mixture for thirty to forty minutes. Dilute with about 75 cc. of water and fit the flask with a wide delivery tube leading to a condenser set downward for distillation. Distil the mixture on an asbestos-centered wire-gauze and collect about 50 cc. of distillate, which consists of ethyl alcohol and water. Pour the residual mixture of *p*-bromoaniline and aqueous solution of potassium acetate into about 100 cc. of cold water and rinse the flask with a little water. The *p*-bromoaniline separates as an oil which crystallizes on standing. Filter the precipitate with suction and wash thoroughly with water.

Dissolve the crude *p*-bromoaniline in a mixture of 75 cc. of water and 5 cc. of concd. hydrochloric acid, add about one gram of decolorizing charcoal (Norite or Darco), and warm on a steam-bath for a few minutes. Filter through a fluted filter to remove the decolorizing charcoal. Pour the filtrate *slowly* with stirring *into* a mixture of 40 cc. of dil. sodium hydroxide solution (10 per cent) and 60–70 g. of clean ice. If performed properly, this procedure results in the precipitation of the *p*-bromoaniline in crystalline form, and not as an oil which later solidifies. Filter the crystals with suction, wash thoroughly with water, and allow to dry. Press between filter papers and dry thoroughly before determining the melting-point. The yield is 5–8 g. The product may be purified by crystallization from dil. alcohol with addition of a little decolorizing charcoal, but a considerable amount is lost in purification.

QUESTIONS

1. To obtain *p*-bromoaniline, why is aniline not brominated directly?
2. What substances are formed by the hydrolysis of: acetamide? acetanilide? *N*-ethyl formamide?
3. How may *m*-bromoaniline be prepared from benzene?

Experiment 40

o-CHLOROTOLUENE[1]

The Sandmeyer Reaction

Preparation of Cuprous Chloride Solution. In a 1-l. round-bottom flask, prepare a solution of 125 g. of powdered copper sulfate crystals ($CuSO_4,5H_2O$) and 35 g. of sodium chloride in 400 cc. of hot water. In a 400–600 cc. beaker prepare a solution of 27 g. of sodium bisulfite and 18 g. of solid sodium hydroxide in about 200 cc. of water, and add this solution with shaking to the hot copper sulfate solution, over a period of five to ten minutes. Cool to room temperature and wash the precipitated cuprous chloride by decantation. The cuprous chloride is obtained as a white powder that darkens on exposure to the air. Dissolve this precipitate by adding 160 g. (135 cc.) of concd. hydrochloric acid and 50 cc. of water and cork the flask to minimize oxidation.

Diazotization of *o*-Toluidine. In a large beaker (about 800-cc.) dissolve 43 g. (43 cc.) of *o*-toluidine in 50 cc. of water and 160 g. (135 cc.) of concd. hydrochloric acid. Cool the mixture to 0° (temperature of the solution, *not* the cooling bath) in an ice and salt mixture and then add 50–75 g. (not over 75 g.) of ice to the cold solution, with good stirring. The salt, *o*-toluidine hydrochloride, separates as a finely divided crystalline precipitate. Prepare a solution of 28 g. of sodium nitrite in 80 cc. of water, and add this solution slowly with vigorous stirring to the suspension of *o*-toluidine hydrochloride. It is advisable to add the sodium nitrite solution through a separatory funnel with the stem extending below the surface of the liquid, to prevent loss of nitrous acid by surface decomposition into oxides of nitrogen (which will appear as brown fumes if the diazotization is not properly carried out). The temperature of the solution must not rise above 5° since this will result in loss of nitrous acid and decomposition of the diazonium salt. The addition of the sodium nitrite solution requires about ten to fifteen minutes. Add a *small* amount of ice from time

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[1] *p*-Chlorotoluene may be prepared by exactly the same procedure, using *p*-toluidine in place of *o*-toluidine.

to time to aid in keeping the temperature sufficiently low. The final volume is about 500–550 cc. Do not allow the resulting diazonium solution to stand any longer than necessary; proceed to the next step. It is often advisable to test for the presence of free nitrous acid (to insure complete diazotization and to avoid an excess of nitrous acid) by the use of potassium iodide-starch paper. Nitrous acid liberates iodine, and the starch is colored blue.

While the diazotization is being carried out, cool the cuprous chloride solution to 0° in an ice and salt mixture. Pour the cold diazonium solution slowly with shaking into the cold cuprous chloride solution. The mixture becomes very thick on account of the precipitation of a double salt of the diazonium chloride with cuprous chloride ($CH_3—C_6H_4—N_2—Cl, CuCl$). Allow the mixture to stand for about ten minutes, then warm slowly on a steam-bath with occasional shaking so that the nitrogen liberated is disengaged from the mass of crystals and there is no loss of material through foaming. The decomposition of the double salt and evolution of nitrogen begin at about 15°.

When the double salt has completely decomposed, steam distil the *o*-chlorotoluene by passing steam into the mixture and attaching a good water-cooled condenser. Separate the layer of *o*-chlorotoluene in the distillate and wash with 30–40 cc. of dil. sodium hydroxide solution (10 per cent). Separate carefully and wash the *o*-chlorotoluene layer with about an equal volume of cold concd. sulfuric acid, then with water to remove the sulfuric acid. Dry with about 5 g. of anhydrous calcium chloride, decant into a small dry distilling flask, and distil on an asbestos-centered wire-gauze. Use an air-cooled condenser and collect the product boiling from 153–158°. The yield is 35–40 g.

➔ **Caution:** Since both the cuprous chloride solution and the diazonium solution decompose on standing, it is important for the success of this preparation to proceed as far as the mixing of these solutions without delay.

QUESTIONS

1. Why is the diazotization carried out at a low temperature?
2. Why is the crude *o*-chlorotoluene washed with cold concd. sulfuric acid?
3. Why does the method used above give a purer product than is obtained by the direct chlorination of toluene?
4. Write equations, indicating all reagents used, for the preparation of the following substances from *o*-toluidine: *o*-cresol; *o*-toluic acid; *o*-tolylhydrazine; *o*-chlorobenzoic acid; an azo dye; toluene.

Experiment 41

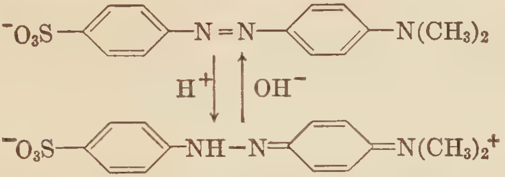
METHYL ORANGE (HELIANTHIN)

Diazotization. In a 500–600-cc. beaker, place 50 cc. of a 5 per cent solution of sodium carbonate, dilute with water to about 100 cc., and add 11 g. of sulfanilic acid. Warm slightly on a steam-bath and if the sulfanilic acid does not completely dissolve add an additional 5–10 cc. of 5 per cent sodium carbonate solution (do not add more than 10 cc.). If necessary, filter the solution with suction to remove the undissolved residue. Carefully weigh out 3.5 g. of sodium nitrite, dissolve it in about 20 cc. of water, and add to the above solution. Cool the solution in a slush of water and ice until the temperature is between 3–5°, then stir vigorously and add drop by drop, a solution of 7 g. (6 cc.) of concd. hydrochloric acid diluted with about 10 cc. of water. Do not allow the resulting diazonium solution to stand any longer than necessary; proceed at once to the next step. It is often advisable to test for the presence of free nitrous acid (to insure complete diazotization and to avoid a large excess of nitrous acid) by the use of potassium iodide-starch paper. In the presence of nitrous acid, iodine is liberated and the starch is colored blue.

Coupling. To 6 g. (6.3 cc.) of dimethylaniline in a test-tube, add 3 g. (3 cc.) of glacial acetic acid and mix thoroughly. To the diazonium salt solution now add quickly, with thorough mixing, the dimethylaniline acetate and allow to stand with occasional stirring for five to ten minutes. Finally make the solution alkaline by adding a solution of 7 g. of solid sodium hydroxide in about 20 cc. of water. This causes the deep red color to change to a yellowish orange. The methyl orange separates at once; it may be made to precipitate more completely by adding about 20 g. of clean salt. Filter the precipitate with suction, using a hardened filter paper, and crystallize the impure product from hot water. Usually about 20–25 cc. of hot water will be required for each gram of material to be crystallized. Cool the hot filtered solution, filter the crystals with suction, wash with alcohol, and finally

with ether. The yield is 10–13 g. of purified methyl orange. Do not attempt to determine the melting-point of this substance.

Dissolve a little methyl orange in water, add a few drops of dil. hydrochloric acid, then make alkaline again with dil. sodium hydroxide solution. Observe the color changes. The effect of acids and alkalies is probably represented by the following structural changes:

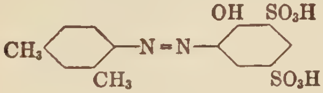


Anion of the Na salt
(alkaline solution)
yellow

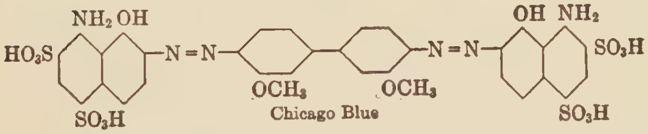
Inner salt
(acid solution)
red

Many types of organic molecules can be used as indicators. All of these have the property of undergoing practically instantaneous change (or changes) in structure in going from acid to alkaline solution, or vice versa, generally within a narrow *p*H range.

Methyl orange belongs to a class of dyes known as "azo colors," which contain the —N=N— group linked to two aromatic nuclei. In addition to the azo group the dyes must contain salt-forming groups such as hydroxyl, amino, sulfonic acid or carboxyl groups (auxochromes) which usually intensify the color and at the same time enable the molecule to attach itself to the fabric, or combine with the mordant to form a lake. Two typical commercial azo dyes are shown below.



Ponceau 2R
(a brilliant scarlet)



Chicago Blue

QUESTIONS

1. What are the most important types of reactions of diazonium compounds?
2. What is meant by chromophore group? auxochrome group? coupling reaction? the Sandmeyer reaction? Give examples of each.

Experiment 42

m-BROMOTOLUENE

Acetylation of *p*-Toluidine—Bromination of *p*-Acetotoluidide—Hydrolysis of Bromoacetotoluidide—Diazotization of Bromotoluidine—Replacement of the Diazonium Group by Hydrogen.

***p*-Acetotoluidide.** Prepare a solution of *p*-acetotoluidide (4-acetamidotoluene) in glacial acetic acid, by refluxing for thirty minutes a mixture of 53.5 g. of *p*-toluidine, 160 g. (152 cc.) of glacial acetic acid and 56 g. (52 cc.) of acetic anhydride. Use this solution directly for the next step without isolating the product.

***m*-Bromo-*p*-Acetotoluidide (3-Bromo-4-Acetamidotoluene).** Remove the condenser and cool the above solution while stirring vigorously, until the temperature has fallen to 45–50°; this may cause a small portion of the product to separate in crystalline flakes. From a separatory funnel allow 82 g. (27 cc.) of bromine to drop slowly into the solution, over a period of about twenty minutes. Adjust the rate of addition of the bromine so that the temperature is held at 45–55°, and continue to stir or shake vigorously during the addition of the bromine. After allowing the reaction mixture to stand for fifteen minutes with occasional shaking, pour it into a vigorously stirred mixture of 500 g. of ice and 500 g. of water, to which 6–7 g. of solid sodium bisulfite has been added. Disintegrate any large lumps of the precipitated 3-bromo-4-acetamidotoluene and filter with suction. Wash the crystals thoroughly with water and press as dry as possible on the filter. Remove the crude product from the funnel and allow to dry until its weight does not exceed 125 g. before proceeding to the hydrolysis. It is unnecessary to purify the crude product at this stage.

3-Bromo-4-Aminotoluene Hydrochloride. Transfer the dried product to a 1-l. round-bottom flask, add 150 cc. of ethyl alcohol (95 per cent), and reflux on a steam-bath until the material has dissolved completely. Through the condenser tube add 125 cc.

of concd. hydrochloric acid to the boiling solution and continue to heat the mixture for three hours. During this time crystals of the amine hydrochloride may separate. Pour the hot mixture into a large beaker and cool thoroughly. Filter the crystals of the hydrochloride with suction, press thoroughly, and wash with two 25-cc. portions of chilled alcohol. The yield is 65–75 g.

3-Bromo-4-Aminotoluene. Suspend the hydrochloride in about 200 cc. of water in a large flask and add, with vigorous shaking, a solution of 35 g. of solid sodium hydroxide in 150 cc. of water. Shake thoroughly for ten minutes to insure a complete liberation of the amine, which separates as a dark heavy oil. Cool to 20°, transfer to a separatory funnel, and separate the heavy layer of crude 3-bromo-4-aminotoluene. The yield is 55–62 g. It is unnecessary to purify the amine before proceeding to the next step; if the pure amine were desired the crude product could be purified by drying over solid sodium hydroxide and distilling under diminished pressure. 3-Bromo-4-aminotoluene distils at 120–122° under 30 mm. pressure; the purified amine solidifies on cooling and melts at 16–18°.

***m*-Bromotoluene.** To a cold mixture of 200 cc. of ethyl alcohol (95 per cent) and 50 cc. of concd. sulfuric acid in a 1.5–2-l. flask, add the crude amine from the previous step (55–62 g.). Cool the solution to 5° and while shaking thoroughly, add slowly from a separatory funnel a solution of 37 g. of sodium nitrite in 65 cc. of water. Keep the reaction mixture cold during the slow addition of the sodium nitrite solution and allow to stand for ten minutes after all of the nitrite has been added, in order to complete the diazotization. At this time a drop of the solution on testing with starch—potassium iodide paper should give an indication of free nitrous acid (immediate blue color). To the *cold* solution add 8–9 g. of powdered copper (copper bronze) which has previously been washed with a little ether. Fit the flask at once with a long reflux condenser and prepare an ice-bath to cool the flask if the reaction becomes too vigorous.

Warm the flask *very cautiously* on a steam-bath until a rapid evolution of gases begins, then chill at once in an ice-bath to prevent the reaction from becoming too vigorous (*Caution—inflammable vapors*). When the reaction has moderated, again warm the flask gently and finally heat for ten minutes on a steam-bath. At

the end of the reaction the color of the solution changes from reddish-brown to yellow. The success of this step depends upon controlling the evolution of gases to avoid loss of material through violent decomposition.

Add about 500 cc. of water to the reaction mixture and steam distil as long as any oily drops pass over. Separate the heavy yellow liquid, wash with two 50-cc. portions of dil. sodium hydroxide solution, once with water, twice with 20-cc. portions of *ice-cold* concd. sulfuric acid, and finally with 20 cc. of saturated sodium bicarbonate solution. Dry with 2–3 g. of anhydrous calcium chloride and decant into a small dry distilling flask. Distil, using an air-cooled condenser, and collect the *m*-bromotoluene boiling at 178–183°. The yield is 25–30 g. Calculate the percentage yield on the basis of the original *p*-toluidine.

QUESTIONS

1. In the preparation of 3-bromo-4-aminotoluene why is it necessary to acetylate *p*-toluidine instead of brominating the amine directly?
2. State the simple rule governing the directive influence of substituents on the benzene ring. Indicate one important exception to this rule.
3. Write a series of equations showing the reactions that would occur if *o*-toluidine were used in place of *p*-toluidine in this experiment.
4. Outline a suitable series of reactions for the preparation of the following compounds in a pure state: *m*-bromophenol from benzene; *m*-nitrotoluene from *p*-toluidine.

Experiment 43

INTERMEDIATE PRODUCTS IN THE REDUCTION OF NITRO COMPOUNDS

Hydrazobenzene. In a 500-cc. round-bottom flask, place 200 cc. of alcohol, 30 g. (25 cc.) of nitrobenzene, and a solution of 15 g. of sodium hydroxide in 35 cc. of water. Connect the flask by means of a rubber stopper with an air-cooled condenser tube about 70–80 cm. in length and 10–12 mm. in diameter. Heat the flask in a steam-bath to about 70–75°, remove from the steam-bath, shake *vigorously* and add about 5–6 g. of zinc dust from a quantity of 50 g. which has been weighed previously. Shake the mixture *vigorously* until the reaction starts. If the reaction becomes violent, check it by dipping the flask in cold water.

When the reaction subsides, heat the flask on the steam bath, remove, and add another portion of zinc dust in the same manner as before, and shake *vigorously*. Continue to warm and add portions of zinc dust until the solution changes from orange red to *pale yellow* in color. About 50 g. of zinc dust will be required; if necessary an additional quantity of 5–15 g. of zinc dust may be used.

When the solution has become pale yellow,[1] add 50–60 cc. of alcohol, heat to boiling, and filter rapidly through a previously warmed Büchner funnel. Wash the sludge of zinc oxide with a small amount of hot alcohol. Transfer the filtrate to a large beaker and cool rapidly in an ice-bath. Filter the crystals of hydrazobenzene with suction, working as rapidly as possible in order to avoid oxidation. The yield is about 20 g.

Do not recrystallize the hydrazobenzene but instead divide the crude crystalline product, after drying for a short time on a filter paper, into two equal fractions to be used in the preparation of benzidine and azobenzene.

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[1] If necessary the operation may be interrupted at this point; if this is done the flask should be fitted with a tight cork. The flask should be opened cautiously since a slight pressure may be developed.

The following directions are based upon a quantity of 10 g. of crude hydrazobenzene in each portion and may be used for 9–11 g. without alteration. For other quantities use proportional amounts of the various reagents.

The Benzidine Rearrangement. Dissolve 10 g. of the crude hydrazobenzene in 100 cc. of ether and add this solution in small portions with shaking to 100 cc. of ice-cold 20 per cent hydrochloric acid (concd. hydrochloric acid diluted with an equal volume of water) contained in a 500-cc. flask. Stopper the flask and shake thoroughly after each addition of the ethereal solution. Benzidine hydrochloride separates out during the reaction. After all of the hydrazobenzene has been introduced, add 50 cc. of concd. hydrochloric acid and allow the reaction mixture to stand for one-half hour in an ice-bath. Filter the benzidine hydrochloride with suction, using a hardened filter paper. Wash the product with 20–25 cc. of 20 per cent hydrochloric acid, followed by two or three 25 cc. portions of ether (Why?).

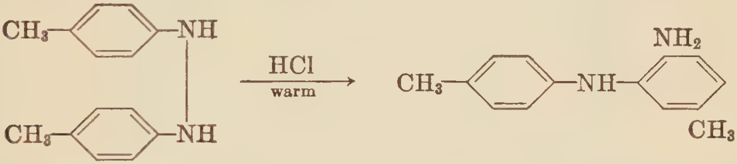
To obtain the free base dissolve the hydrochloride in 200 cc. of warm water, filter the solution and cool rapidly to 20°. Pour the solution with stirring into a mixture of 50 cc. of 10 per cent sodium hydroxide solution and 200 g. of ice, contained in a large beaker. The benzidine separates out in grayish-white flocks. Filter with suction on a large Büchner funnel and wash thoroughly with distilled water. The crude product can be crystallized from a very small amount of alcohol or from hot water (about 15 cc. of alcohol, or 40 cc. of water, will be required for each gram of benzidine). The yield is 4–5 g.

Azobenzene from Hydrazobenzene. Prepare a solution of sodium hypobromite by allowing 10 g. of bromine (3.2 cc.) to drop with constant shaking into 75 cc. of *ice-cold* 8 per cent sodium hydroxide solution (cooled in an ice-bath). Dissolve 10 g. of the crude hydrazobenzene in 60 cc. of ether, transfer the solution to a small separatory funnel, and add the sodium hypobromite solution in small portions. After all of the hypobromite has been added, shake the reaction mixture for ten minutes longer. Draw off the aqueous layer and pour the ethereal layer into a 200-cc. distilling flask. Distil off the ether by heating very gently on a steam-bath. Dissolve the warm liquid residue in 35 cc. of alcohol, transfer to a 200-cc. beaker, and heat to boiling on a steam-bath. Add water

dropwise to the hot solution until the azobenzene begins to separate, then add 3–4 cc. of alcohol and chill the mixture thoroughly. Filter the bright orange crystals with suction and wash with a small quantity of ice-cold 50 per cent alcohol. The yield is 7–9 g.

The benzidine rearrangement takes place readily with substituted hydrazo compounds only if the *p*-positions to the NH groups are unsubstituted and if the other hydrogens in the benzene rings are not unfavorably substituted; thus, *o,o′*-dimethoxy hydrazobenzene, and *o,o′*-dimethyl hydrazobenzene which are formed from *o*-nitroanisol and *o*-nitrotoluene are converted smoothly to dianisidine (4,4′-diamino-3,3′-dimethoxybiphenyl) and tolidine (4,4′-diamino-3,3′-dimethylbiphenyl) which are important dye intermediates for substantive azo dyes (which dye directly without a mordant).

If one or both of the *p*-positions of the hydrazo compound is substituted, the rearrangement may proceed only half-way and yield an *o*- or *p*-amino derivative of diphenylamine (called *o*- and *p*-semidines), or it may occur in both rings and give an *o,p′*-diaminobiphenyl derivative (called a diphenyline base). Thus, the hydrazo compound from *p*-nitrotoluene undergoes rearrangement to give an *o*-semidine:



p-Hydrazotoluene

an ortho-semidine

By reducing nitrobenzene with zinc in neutral or faintly acid medium, phenylhydroxylamine (C_6H_5NHOH) can be obtained. The latter undergoes rearrangement on treatment with strong sulfuric acid to give the sulfate of *p*-aminophenol:

$$C_6H_5{-}NH{-}OH \longrightarrow HO{-}C_6H_4{-}NH_2$$

The latter is a photographic developer, and also an important intermediate for the preparation of synthetic drugs and dyes.

QUESTIONS

1. What reducing agents are used in the preparation of primary aromatic amines from nitro compounds?
2. Write the names and formulas of the substances which are formed by the reduction of nitrobenzene with zinc dust in alkaline solution; in neutral solution.
3. What is formed by the action of the following reagents on phenylhydroxylamine: concd. hydrochloric acid? cold concd. sulfuric acid? potassium dichromate and dil. sulfuric acid? nitrous acid?
4. What relation does azobenzene bear to the azo dyes? Is azobenzene a dye?
5. Why is benzidine of particular importance in the preparation of azo dyes?

Experiment 44

DISTILLATION UNDER DIMINISHED PRESSURE (VACUUM DISTILLATION)

Since the boiling-point of a substance is decreased by diminishing the pressure upon its surface, it is possible to effect distillation at appreciably lower temperatures by using a closed system in which the internal pressure has been reduced to 10–30 mm. This procedure is useful for the purification of liquids (or low-melting solids) that are decomposed at elevated temperatures or are oxidized appreciably during distillation in the air. It is widely used in the laboratory and in commercial practice.

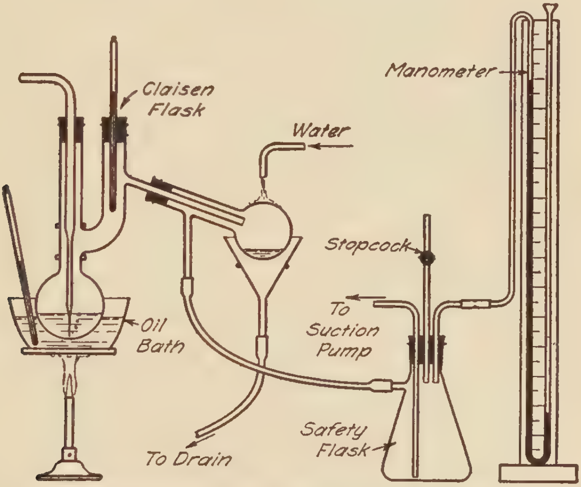


Fig. 22.—Apparatus for Distillation under Diminished Pressure.

On a laboratory scale, vacuum distillations are usually carried out in a special type of flask (Claisen flask) provided with two necks, one serving to hold a capillary tube and the other to hold a thermometer. The principal purpose of this special construction is to diminish the chance of mechanical contamination of the distillate from frothing or violent bumping. Both of these difficulties are more troublesome in vacuum distillation than in ordi-

nary distillation. The size of the Claisen flask should be such that it is not quite half-filled by the liquid to be distilled. The flask is usually heated in an oil-bath or sand-bath to insure regular heating, and to allow observation of the temperature of heating. The temperature of the bath is usually 15 to 25° higher than that of the distilling vapor.

To promote regular ebullition and to avoid bumping, a fine stream of air bubbles is introduced at the bottom of the flask through a thin flexible capillary tube. Chips of porous clay plate are not effective in vacuum distillation. The capillary is prepared by drawing out a piece of ordinary glass tubing, 7–8 mm. in diameter, to capillary dimensions and drawing out this first capillary, in a small luminous flame, to an extremely fine and flexible capillary thread. The capillary thread is tested by blowing into the tube while the thread is held under alcohol or ether; it should emit a fine stream of very minute bubbles. The top of the tube which bears the capillary should be bent at right angles in order to facilitate adjustment of the depth of the capillary tube so that it will reach exactly to the bottom of the distilling flask.

For receivers, ordinary distilling flasks are used. A number of these, sufficient to receive all of the fractions, are prepared before the distillation is begun. The necks of all of the receiving flasks must be of about the same dimensions so that they will all fit tightly on the stopper of the side-tube of the Claisen flask. The delivery tube of the Claisen flask should reach just into the bulb of the receiver. In order to simplify the apparatus the ordinary condenser is omitted; instead, the receiver is supported above a large funnel and is cooled directly by a jet of cold water. This type of cooling is satisfactory for liquids that distil above 50°; for liquids that distil below this temperature a more elaborate cooling device is necessary.

All connections in the apparatus must be tight, and special attention must be given to the quality and size of the tubing and stoppers. Rubber stoppers are often used because they simplify the preparation of tight joints, but in many cases they are likely to contaminate the distillate with impurities. Clean corks of good quality are preferable although their use requires more skill and care to obtain tight connections. The corks should be rolled and pressed before use and should be of such size that not more than

one-half (nor less than one-quarter) of the cork projects into the neck of the opening. Their porosity can be diminished and tight joints may be obtained by applying a *thin* coating of collodion after the system has been evacuated. The external pressure serves to force the collodion into the pores of the cork.

Evacuation of the system is effected by means of a water pump or a motor-driven oil pump. A good water pump is capable of evacuating a small system to a pressure of 25 mm. or less, using water at 20°; with colder water, pressures as low as 8–10 mm. can be obtained.[1] The water pump is connected with the apparatus through a safety-flask provided with a stop-cock. The purpose of this arrangement is to prevent water from being drawn back into the distilling system or the manometer. If water begins to flow back into the apparatus, it may be checked by opening the stopcock slightly and allowing the pressure in the system to increase.

The following points should be observed in carrying out a vacuum distillation:

1. Test the completely assembled apparatus before placing the liquid in the Claisen flask, to detect leaks and to make certain that all of the parts of the apparatus will withstand the external pressure. *Use goggles to protect the eyes.*

2. In using a water pump turn on the water to the full pressure, otherwise water may be sucked back into the safety flask.

3. In releasing the vacuum in the distilling flask open the stopcock on the safety-flask and gradually allow the pressure to reach atmospheric pressure in the apparatus before shutting off the water pump.

4. When changing receivers remove the flame from beneath the bath, and allow the distilling flask to cool slightly before releasing the vacuum (by lowering the bath or raising the flask from the bath). After the receiver has been changed the system should be evacuated again before the heating is continued.

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[1] The pressure in the system can be measured by means of a closed or an open tube mercury manometer. With a closed tube manometer the difference in the mercury levels gives directly the pressure within the system. Although these manometers are less cumbersome, they are difficult to fill properly and give erroneous readings if the closed tube contains bubbles of air. With an open tube manometer it is necessary to subtract the net height of the mercury in the manometer from the barometric pressure.

Purification of Benzaldehyde. Purify a 60 g. (58 cc.) sample of technical benzaldehyde in the following way. Wash with two 20-cc. portions of sodium carbonate solution (10 per cent), then with water, and dry over 5–10 g. of anhydrous magnesium sulfate. It is advantageous to add a few small crystals of hydroquinone or catechol (anti-oxidants) during the drying operation. Decant through a fluted filter (or a small plug of cotton) into a Claisen flask of suitable size and distil under diminished pressure (preferably below 30 mm.) in the manner described above. Place a few crystals of hydroquinone or catechol (anti-oxidants) in the receiving flask in which the purified benzaldehyde is collected. To determine the boiling-point of benzaldehyde under the particular pressure in your apparatus, prepare a graph from the following boiling-point data for benzaldehyde: 180°/760 mm., 95°/50 mm., 87°/35 mm., 80°/25 mm., 70°/15 mm., 62°/10 mm.

In distilling a substance easily oxidized by atmospheric oxygen, it is advantageous to use an extremely fine capillary thread for the introduction of bubbles. For more refined work a fine stream of an inert gas (hydrogen, nitrogen, carbon dioxide) would be used in place of air.

Auto-oxidation. In common with many oxidizable substances, benzaldehyde is capable of combining directly with oxygen of the air and is converted eventually to benzoic acid. This property of reacting directly with molecular oxygen is called auto-oxidation.

The process of auto-oxidation is extremely sensitive to the effect of catalysts, which are considered to act upon an unstable intermediate complex of "peroxide" character that is the initial step of oxidation. Catalysts that accelerate auto-oxidation are called pro-oxidants; those which retard or inhibit auto-oxidation are called *anti-oxidants.* The latter find important technical application for the preservation of organic materials; for example, the deterioration of rubber is greatly retarded by the incorporation of anti-oxidants. Likewise, the auto-oxidation of benzaldehyde can be effectively inhibited by the addition of a trace (less than 0.1 per cent is sufficient) of hydroquinone or catechol.

Although the action of anti-oxidants is somewhat specific, certain classes of compounds are active toward a variety of oxidizable substances. The common anti-oxidants include *o*- and *p*-dihydroxybenzenes and aminophenols, many amines, thioamides, mercaptans, and sulfides.

QUESTIONS

1. Write equations for the technical method of preparing benzaldehyde. What substances might be present as impurities in technical benzaldehyde?
2. Explain the fact that benzaldoxime exists in two different forms.

Purification of Ethyl Acetoacetate. Purify a 60 g. (60 cc.) sample of technical acetoacetic ester [1] in the following way. Wash first with a small amount of saturated sodium bicarbonate solution to remove acetic acid, then with water, and dry over 5–10 g. of anhydrous magnesium sulfate or potassium carbonate. Decant through a fluted filter (or a small plug of cotton) into a Claisen flask of suitable size and distil under diminished pressure (preferably below 30 mm.) in the manner described above.

During the distillation of the low-boiling fraction, containing ethyl acetate, the high vapor pressure of the latter may increase the pressure in the system above 30 mm. If this occurs, the distillation of the first fraction may be carried out at a higher pressure, but the pressure should be maintained below 30 mm. for the distillation of the remaining fractions. To obtain the correct boiling-point of ethyl acetoacetate under the particular pressure in your apparatus prepare a graph from the following boiling-point data for ethyl acetoacetate: 180°/760 mm., 100°/80 mm., 97°/60 mm., 88°/30 mm., 78°/18 mm., 74°/14 mm., 71°/12 mm.

Collect the purified ethyl acetoacetate over an interval of 5–6°, determined from the above information and calculate the percentage recovery from the crude product.

Enol Test. Suspend a few drops of purified ethyl acetoacetate in 5 cc. of water and add a few drops of a 5 per cent solution of ferric chloride. Shake thoroughly and observe.

Carry out the enol test with 5 cc. portions of a dil. aqueous solution of the following substances: phenol, catechol (1,2-dihydro-oxybenzene), allyl alcohol, acetone.

QUESTIONS

1. Write balanced equations, including all intermediate steps, for the preparation of ethyl acetoacetate from ethyl acetate.
2. Write formulas for the ester produced by the action of metallic sodium on: ethyl propionate; a mixture of ethyl benzoate and ethyl acetate.
3. Explain what is meant by the term, tautomerism, and illustrate with ethyl acetoacetate.
4. Write formulas for the possible tautomeric forms of the following: acetaldehyde; acetone; ethyl acetate; phenol.

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[1] Technical ethyl acetoacetate usually contains some ethyl acetate and a little acetic acid. Since ethyl acetoacetate decomposes to some extent on heating to its boiling-point at atmospheric pressure [with the formation of dehydracetic acid ($C_8H_8O_4$)] it is purified by distillation under diminished pressure. It may also be purified by *rapid* distillation at atmospheric pressure.

Experiment 45

BENZYL ALCOHOL AND BENZOIC ACID

The Cannizzaro Reaction

Dissolve 27 g. of solid potassium hydroxide in 25 cc. of water, cool to 20°, and add the solution to 30 g. (29 cc.) of freshly distilled benzaldehyde. Shake until an emulsion is formed and allow to stand for ten to twenty hours. Add just enough water to dissolve the precipitated potassium benzoate, and extract the solution with three or four 30-cc. portions of ether. Save the aqueous solution and the ether extracts.

Combine the ether extracts and distil the ether from a steam-bath until the volume is about 25–30 cc. Cool and shake the ether solution several times with 5-cc. portions of an approximately saturated solution of sodium bisulfite. Wash the ether with 5–10 cc. of 10 per cent sodium carbonate solution, dry with 4–5 g. of anhydrous magnesium sulfate, and distil the ether from a steam-bath. Distil the residual benzyl alcohol from a small distilling flask and collect the portion boiling from 200–206°. The yield is 6–8 g.

Pour the aqueous solution of potassium benzoate with stirring *into* a mixture of 75 cc. of concd. hydrochloric acid, 75 cc. of water, and about 100 g. of ice. Filter the precipitated benzoic acid, wash once with water and crystallize from water. The yield is 12–13 g.

The Cannizzaro reaction is applicable to substituted aromatic aldehydes with the exception of *o*- and *p*-hydroxy derivatives. In many instances the alcohol is the only desired product. Under these circumstances, it is possible to use what is known as a "crossed" Cannizzaro reaction. Formaldehyde is added to the reaction mixture and being more sensitive to oxidation than the aromatic aldehyde, the aromatic aldehyde is converted in good yield to the alcohol and the formaldehyde goes to formic acid:

$$C_6H_5CH{=}O + CH_2{=}O + NaOH \longrightarrow C_6H_5CH_2OH + HCO_2Na$$

QUESTIONS

1. Why is it advisable to treat the ethereal solution of benzyl alcohol with sodium bisulfite solution?

2. How may the conditions of the reaction and the reagent be modified to obtain benzyl benzoate as the principal product?

Experiment 46

BENZALACETOPHENONE (CHALCONE)

The Claisen Condensation

In a 200-cc. flask place a solution of 5 g. of sodium hydroxide in 45 cc. of water and 25 cc. of alcohol. Pour into this mixture, 12 g. (12 cc.) of freshly distilled acetophenone, and immediately cool the flask in ice-water. Shake [1] the mixture thoroughly and add 10.5 g. (10 cc.) of freshly purified and redistilled benzaldehyde (see page 289). Keep the temperature at about 25° (above 15° and below 30°) and continue to shake the mixture from time to time over a period of an hour or two. Then set aside in a cool place or chill in an ice-salt bath for at least one-half hour.

It is advisable, but not essential, to start the crystallization of the product by inoculating with a few small crystals of benzalacetophenone about thirty minutes after the materials are mixed.

Filter the product with suction and wash thoroughly with water, until the washings are neutral to litmus. Finally wash with 5–10 cc. of alcohol which has been cooled previously in an ice-salt mixture. Crystallize the crude product from alcohol (about 4–5 cc. of alcohol will be required for each gram of benzalacetophenone). The yield is 15–17 g.; m.p. 56–57°.

➔ **Caution:** Benzalacetophenone should be handled carefully since it acts as a skin irritant; certain individuals are particularly sensitive to it.

QUESTIONS

1. What would be formed if acetone were substituted for acetophenone in the above experiment?
2. What special type of unsaturated system is present in benzalacetophenone? Write equations showing the mechanism of addition of hydrogen chloride to benzalacetophenone.
3. What products are obtained by the action of the following reagents on benzalacetophenone: hydrogen cyanide; phenylmagnesium bromide (followed by dil. acid); hydroxylamine?
4. State the number and nature of the stereoisomeric forms of: benzalacetophenone; benzalacetophenone dibromide.

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[1] If mechanical stirring is available it is desirable to employ it for this operation; for a simple stirring device see page 383.

Experiment 47

BENZOIN AND BENZIL

Benzoin. In a 500-cc. round-bottom flask place 25 g. (24 cc.) of freshly distilled benzaldehyde, 35 cc. of alcohol, and a freshly prepared solution of 2 g. of sodium cyanide (*Caution*) in 25 cc. of water. Adjust a reflux condenser and reflux gently on the steam-bath for forty-five minutes. Cool the contents of the flask and filter the crystals with suction. Wash with 25–30 cc. of cold 50 per cent alcohol, then with several portions of water. Press as dry as possible on the filter and allow to dry [1] in the air. The yield is 18–22 g.

To obtain pure benzoin the crude product obtained above can be crystallized from alcohol (about 8 cc. of alcohol will be required for each gram of benzoin). It is unnecessary to purify the benzoin for use in the preparation of benzil or benzilic acid.

Benzil. In a 200-cc. round-bottom flask place 16 g. of crude benzoin obtained in the preceding experiment, and add 57 g. (40 cc.) of concd. nitric acid. Heat on a steam-bath, preferably in a hood, until the evolution of oxides of nitrogen has ceased (about two hours). Pour the reaction mixture with stirring into four or five times its volume of ice-water and filter with suction the crude benzil which is precipitated in small yellow lumps. Break up the lumps with a porcelain spatula and wash several times with water to remove the nitric acid. Allow to dry in the air and crystallize from alcohol (about 2.5–3 cc. of alcohol will be required for each gram of benzil). The yield is 10–12 g.

QUESTIONS

1. Compare the benzoin condensation with the aldol condensation, the Cannizzaro reaction, the cyanohydrin reaction.
2. What is benzopinacol and how is it formed?
3. What would be the product of the action of an excess of methylmagnesium bromide upon benzoin? benzil?
4. What is the benzilic acid rearrangement?

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[1] If Experiment 48a (benzilic acid) is to be performed, the product should not be dried but used directly, after pressing on the filter.

Experiment 48a

BENZILIC ACID

In a 10-cm. evaporating dish prepare a solution of 25 g. of solid sodium hydroxide and 6 g. of sodium bromate (or 6.5 g. of potassium bromate) in 45 cc. of water. To the solution add in portions the moist benzoin from the preceding experiment (corresponding to 20–22 g. of dry benzoin). During and after the addition of the benzoin heat the reaction mixture on a steam-bath (85–90°) and stir continually. Do not heat the mixture to boiling since this will cause the formation of a large amount of benzohydrol (diphenylcarbinol). Add small quantities of water from time to time to prevent the mixture from becoming too thick. Continue the heating and stirring until a small test portion is completely or almost completely soluble in water. This usually requires about two hours.

Dilute the mixture with 200 cc. of water, allow to stand, and filter off the oily or solid impurity (benzohydrol). To the filtrate add slowly, with stirring, 40 per cent sulfuric acid (prepared by adding 20 cc. of concd. sulfuric acid to 60 cc. of water) to a point just short of the liberation of bromine.[1] Usually about 65 cc. of sulfuric acid will be required. Filter the product with suction, wash with water, and dry. The yield is 17–20 g. and the product is usually of such high purity that recrystallization is unnecessary. Benzilic acid can be purified by crystallization from hot benzene (about 6 cc. of solvent is required per gram of the acid).

QUESTIONS

1. What intermediate product is produced in this reaction before the benzilic acid rearrangement occurs?
2. Write an equation to explain the formation of benzohydrol as a by-product in this reaction.
3. Write equations for the action of the following reagents upon benzilic acid: phosphorus pentachloride; hydriodic acid and phosphorus.

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[1] To minimize the danger of passing the end-point it is advisable to set aside in a test-tube, 8–10 cc. of the filtrate and add sulfuric acid to the remainder until a *trace* of bromine is liberated. This is removed by adding the small portion of the solution from the test-tube.

Experiment 48b

BENZILIC ACID

The Benzilic Acid Rearrangement

In a small round-bottom flask place a solution of 10 g. of potassium hydroxide in 20 cc. of distilled water, add 25 cc. of alcohol, and mix thoroughly. To this solution add 10 g. of *pure* benzil (a deep bluish-black color is developed) and boil the mixture on a steam-bath under a reflux condenser for ten to fifteen minutes. Pour the contents of the flask into a small porcelain dish and allow to cool and to stand, preferably for several hours. The potassium salt of benzilic acid precipitates in crystalline form. After the separation is complete, filter the crystals with suction and wash with a small amount of alcohol. The alcoholic mother-liquors, on standing overnight, will yield a small additional quantity of the salt.

Dissolve the potassium salt in about 300 cc. of water and add slowly, with stirring, *five drops* of concd. hydrochloric acid (sp. g. 1.19). The precipitate produced thus is colored red-brown and is slightly sticky. Filter off this precipitate; if the procedure has been carried out correctly the filtrate is almost colorless or only pale yellow. Pour the filtrate, with stirring, into a solution of 15 cc. of concd. hydrochloric acid in 100 cc. of water and filter the precipitated benzilic acid with suction. Wash thoroughly with cold water, until free from chlorides, and allow to dry. The yield is 8–9 g. of a product which is usually a light pink or yellow in color. The crude product is purified by crystallization from hot benzene (about 6 cc. of benzene is required per gram). The yield of purified product is 6–8 g.

QUESTIONS

1. What intermediate product is produced in this reaction before the benzilic acid rearrangement occurs?
2. Write equations for the action of the following reagents upon benzilic acid: phosphorus pentachloride; hydriodic acid and phosphorus.

Experiment 49

DIPHENYLACETIC ACID

Place 50 cc. of glacial acetic acid, 3 g. of red phosphorus, and 1 g. of iodine in a 200-cc. round-bottom flask. Allow the mixture to stand for fifteen minutes, then add 1 cc. of water and 18 g. of benzilic acid. Attach a reflux condenser and boil the mixture continuously for two and one-half to three hours. After the reaction is complete, filter the hot mixture to remove the excess of red phosphorus. Pour the hot filtrate *slowly* into a cold, well-stirred, filtered solution of 4–5 g. of sodium bisulfite in 200 cc. of water. This procedure removes the excess of iodine and precipitates the diphenylacetic acid as a fine white or slightly yellow powder. Filter the product with suction, wash with cold water, and press as dry as possible on the filter. Purify the product by crystallization from hot 50 per cent alcohol, with the addition of 1–2 g. of decolorizing charcoal. About 6–7 cc. of solvent will be required for each gram of the product. The yield is 12–14 g.

Control test: Treat a little of the product with cold concd. sulfuric acid. If any unreduced benzilic acid is present a red color will be observed.

QUESTIONS

1. Explain why a relatively small quantity of iodine suffices for the reduction of a considerable quantity of benzilic acid.
2. What product would be obtained by the action of red phosphorus and bromine on benzilic acid, in the absence of water? What would result if this product were treated with water?
3. What product would be obtained upon nitrating diphenylacetic acid?

Experiment 50

CINNAMIC ACID[1]

The Perkin Reaction

In a dry 200-cc. flask place 12 g. of *freshly fused* and pulverized potassium acetate.[2] This is prepared by melting ordinary potassium acetate in a porcelain dish and heating gently, with occasional stirring, until no more water vapor is evolved and the salt is completely fluid. After cooling, the solid mass is ground quickly in a mortar and transferred to a tightly corked bottle until needed. To the potassium acetate add 30 g. (28 cc.) of acetic anhydride and 21 g. (20 cc.) of freshly distilled benzaldehyde. Mix the materials thoroughly and provide the flask with an air-cooled reflux condenser about 600 mm. in length and 10 mm. in diameter. Heat the reaction mixture in an oil-bath at 155–160° for one hour and then increase the temperature of the bath to 160–170°. Continue to heat the reaction mixture at 160–170° for three to three and one-half hours.

If the heating is interrupted the reaction mixture should be protected from atmospheric moisture by means of a calcium chloride tube.

While the reaction mixture is still hot, pour the contents of the flask into a 2-l. round-bottom flask and rinse the reaction flask with two 100-cc. portions of boiling water. Add 300–350 cc. of water and steam distil the mixture until all of the unchanged benzaldehyde has been removed. The distillate can be discarded.

Add enough water to the contents of the flask to bring the volume to about 1200 cc. and heat to boiling. Cool slightly, add 3–4 g. of decolorizing charcoal (Norite), and boil the solution gently for five to ten minutes. Filter the hot solution rapidly through a fluted filter. Heat the filtrate to the boiling point, add 12–14 cc. of concd. hydrochloric acid and cool the solution with stirring. After the cinnamic acid has crystallized completely, filter

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[1] Furylacrylic acid ($C_4H_3O—CH═CH—CO_2H$) may be prepared by the same procedure, using an equivalent quantity of furfural in place of benzaldehyde.

[2] The equivalent quantity of fused sodium acetate (10 g.) can be used in place of potassium acetate, but if sodium acetate is used it is advisable to heat the reaction mixture for two hours longer, since the progress of the reaction is slower.

with suction and wash the crystals with several small portions of cold water. Allow the acid to dry completely before taking the melting-point and weighing the product. If the cinnamic acid is not sufficiently pure it should be recrystallized from hot water. The yield is 12–15 g.

Perkin's condensation is applicable to aromatic aldehydes (and some aliphatic aldehydes) and aliphatic acid anhydrides with two hydrogens on the α-carbon atom. If the α-carbon in the anhydride is disubstituted, as in *iso*-butyric anhydride, the reaction leads to an hydroxy acid which cannot undergo dehydration to an unsaturated acid:

$$C_6H_5CH{=}O + [(CH_3)_2CH{-}CO]_2O \longrightarrow C_6H_5CHOHC(CH_3)_2CO_2H$$

With three substituents on the α-carbon, no reaction occurs.

Substituted benzaldehydes containing alkyl, halogen, or nitro groups also take part readily in the Perkin condensation. Alkoxy derivatives usually give somewhat lower yields (25–35 per cent), and *p*-dimethylaminobenzaldehyde gives very unsatisfactory results. The condensation may also be carried out with cinnamaldehyde ($C_6H_5{-}CH{=}CH{-}CH{=}O$) and with furfural.

The question of whether the reaction takes place with the acid anhydride or the salt of the acid is a rather complex one. It seems quite likely that the salt and anhydride interact to form an addition product in which enolization of the hydrogens on the α-carbon atom is promoted, and then condensation with benzaldehyde takes place.

An interesting extension of the Perkin reaction, known as the Erlenmeyer synthesis, involves the use of acyl derivatives of aminoacetic acid ($CO_2H{-}CH_2{-}NH{-}COR$) to give derivatives of α-aminocinnamic acid.

Aromatic aldehydes in general enter into analogous condensations with active methylene compounds. Condensation will take place readily with malonic acid, with diethyl malonate, ethyl acetoacetate, or ethyl cyanoacetate, in the presence of secondary amines as catalysts (Knoevenagel reaction); with nitromethane; with methyl or methylene ketones such as acetone, acetophenone, desoxybenzoin, etc., in the presence of sodium ethoxide.

QUESTIONS

1. Write equations for the reaction of benzaldehyde and malonic ester (or malonic acid); an excess of acetone; acetaldehyde. How could cinnamic acid be obtained from each of these products?
2. How can the following substances be prepared from cinnamic acid: phenylpropionic acid? phenylpropiolic acid? β-bromostyrene? cinnamoyl chloride?
3. What is coumarin and how can it be prepared?
4. What acid would be obtained by heating benzaldehyde with potassium propionate and propionic anhydride?
5. What is meant by *cis*- and *trans*-cinnamic acids?

Experiment 51

β-BROMOSTYRENE

Dissolve 15 g. of dry cinnamic acid in 100 cc. of hot carbon tetrachloride in a 500-cc. round-bottom flask and cool rapidly to obtain a fine suspension of crystals. Provide the flask with a calcium chloride tube and a small separatory funnel (with a good stopcock). In the separatory funnel place a solution of 19 g. (6 cc.) of bromine in 25 cc. of carbon tetrachloride and allow this to drop in slowly, at room temperature, while the flask is being vigorously shaken. It is advisable to carry out the addition of bromine in the presence of sunlight, or in the vicinity of a powerful electric light. After all of the bromine has been added, allow the mixture to stand for fifteen minutes. Cool in an ice-bath and filter the phenyl-α,β-dibromopropionic acid with suction. Wash the precipitate with 25–30 cc. of cold carbon tetrachloride. This crude product, weighing 25–30 g., is used directly for the next step.

Place the crude dibromo acid in a 1-l. round-bottom flask and add 120 cc. of 95 per cent alcohol and a solution of 30 g. of potassium acetate in 75 cc. of water. Shake the mixture thoroughly, adjust a reflux condenser, and heat to gentle boiling (preferably on a steam-bath). Shake the mixture occasionally, and continue to reflux gently for four hours. The product, bromostyrene, separates as a heavy oil upon cooling. Dilute with water to about 500 cc. total volume, separate the heavy oil, and extract the upper aqueous liquid with two 25-cc. portions of carbon tetrachloride. Combine the oily layer and the carbon tetrachloride extract and wash with saturated sodium bicarbonate solution until all acid has been removed. Wash once with water, dry over 4–5 g. of anhydrous calcium chloride, and distil off the carbon tetrachloride. Distil the residual bromostyrene under reduced pressure (see page 283); b.p. 108° at 20 mm., 116–117° at 35 mm. The yield is 11–12 g.

QUESTIONS

1. Compare the behavior of α-, β-, and γ-bromobutyric acids toward alkalies.
2. How may bromostyrene be converted into phenylacetylene?

Experiment 52

TRIPHENYL CARBINOL

The Grignard Reaction [1]

➔ **Caution:** It is advisable to have a bath of ice and water at hand during this preparation as the reaction may start suddenly with vigorous ebullition of the ether. Take care that no flame is nearby.

Preparation of Phenyl Magnesium Bromide Solution. In a 200-cc. round-bottom flask provided with a long reflux condenser, place 2.4 g. of magnesium turnings (*carefully weighed*) and about 75 cc. of *absolute* ether.[2] In the top of the condenser, support a small cylindrical separatory funnel by means of a one-hole cork provided with one or two slots to allow the passage of air. In the funnel place 15 g. (10 cc.) of bromobenzene, and allow 2–3 cc. of the bromobenzene to flow into the flask. If a reaction (accompanied by ebullition of the ether) does not start at once, warm the flask gently in a bath of warm water. If the reaction does not start after this treatment, add a very small crystal of iodine, or a small quantity of a previously prepared Grignard reagent. It is absolutely essential for the success of the experiment that the reaction begin before the remainder of the halogen compound is added.

When the reaction has started, allow the remainder of the bromobenzene to flow drop by drop into the reaction mixture, at such a rate that the ether refluxes gently without external heating. After all of the halide has been added, reflux the mixture gently for one-half hour on a water-bath or steam-bath. Do not reflux so vigorously that the ether vapors traverse the condenser.

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[1] In Grignard reactions it is essential that the reagents be free from alcohol and water, and the apparatus and corks perfectly clean and dry. It is wise to rinse the apparatus, after the usual drying, with a little anhydrous ether.

[2] Ether which is used as the solvent must be carefully purified to remove impurities (alcohol and water) which are present in the technical product. The procedure which is used in the preparation of absolute, anhydrous ether consists in: (1) washing with strong calcium chloride solution; (2) preliminary drying with calcium chloride; (3) drying with phosphorus pentoxide; (4) distillation, with precautions to protect the product from atmospheric moisture. In some laboratories absolute ether is dried over metallic sodium instead of phosphorus pentoxide. A good quality of anhydrous ether can now be obtained on the market.

Reaction of Phenyl Magnesium Bromide with Ethyl Benzoate. Remove the flask containing the Grignard reagent from the steam-bath and cool to room temperature or below. In the separatory funnel place a solution of 8 g. (8 cc.) of pure ethyl benzoate in about 25 cc. of *absolute* ether. Allow this ethereal solution to flow into the Grignard solution, while thoroughly mixing the two solutions by shaking. Cool the flask from time to time if necessary. When all of the ethyl benzoate has been added, allow the mixture to stand at room temperature for about half an hour. (In the meantime arrange an apparatus for steam distillation.) Pour the contents of the flask (as completely as possible) into a mixture of about 50 g. of ice, 100 cc. of water, and 5–6 cc. of concd. sulfuric acid, contained in a large flask. Shake the mixture thoroughly to complete the decomposition of the organo-magnesium complex, and rinse the reaction flask with this mixture in order to obtain the product which adheres to the walls of the flask. Add about 75 cc. of *ordinary* ether to aid in extracting the product completely, since triphenyl carbinol is but slightly soluble in ether.

Separate the ethereal layer, wash twice with 20–30-cc. portions of dil. sulfuric acid (about 5–10 per cent), once with water, and then with 20–30 cc. of water containing about 0.5 g. of sodium bisulfite (to remove any iodine used to start the reaction). Place the solution in a large round-bottom flask (to be used subsequently for steam-distillation). Attach a condenser set for distillation, and distil off the ether from a steam-bath. To the residue in the flask add about 50 cc. of water, and steam distil the mixture as long as any organic material distils. Most of the impurities are volatile with steam, whereas triphenyl carbinol is not volatile. Cool the distillation flask, filter the crystals of crude product, and press as dry as possible on the suction filter. Crystallize from a small amount of hot ethyl alcohol. The yield is 7–9 g.

QUESTIONS

1. Outline a satisfactory method of purifying the following materials for use in a Grignard reaction: *n*-butyl bromide; *o*-bromotoluene; benzaldehyde; acetone.

2. What is meant by the term, oxonium compound? Explain the role of ether in the Grignard reaction.

3. Write equations for the action of the following substances on phenyl magnesium bromide: carbon dioxide; ethyl formate; acetone; ethyl alcohol.

Experiment 53

n-BUTYL CYANIDE (*n*-VALERONITRILE)

In a 500-cc. round-bottom flask, place 39 g. of powdered sodium cyanide (*handle with great care*), add 100 cc. of water, and warm on a steam-bath for about five minutes. Add a solution of 89 g. (70 cc.) of *n*-butyl bromide in 89 g. (115 cc.) of methyl alcohol, and immediately attach a reflux condenser. Add a few chips of clay plate and boil gently for twenty-five to thirty hours on a steam-bath. Cool the reaction mixture to room temperature and filter with suction, to remove the crystalline sodium bromide which has separated. Wash the crystals of sodium bromide with about 25 cc. of methyl alcohol, and add this to the original filtrate which contains the organic products.

Transfer the filtrate to a 500-cc. round-bottom flask and distil off the methyl alcohol through an effective fractionating column (a two-bulb Wurtz column filled with broken glass tubing, or a 15–20 cm. Hempel column filled with glass beads, etc.). It is necessary to distil slowly and regularly so that a good separation is obtained; otherwise a low yield results. Collect the methyl alcohol fraction until the temperature of the vapors reaches 83°. This fraction contains most of the methyl alcohol and only a very small amount of the *n*-butyl cyanide (and a trace of *n*-butyl isocyanide which gives it a disagreeable odor). If the fractionation has been effective, this fraction may be discarded; otherwise, it may be necessary to refractionate the first distillate.

Cool the flask slightly, remove the fractionating column, and add about 200 cc. of water. Connect the flask by means of a wide, bent delivery tube to a condenser set downward for distillation, and distil on an asbestos-centered wire-gauze. Distil the mixture as long as any water-insoluble material passes over. The distillate contains the crude *n*-butyl cyanide and water, and separates into two layers.

The residue in the flask contains unreacted sodium cyanide, some sodium bromide, and high-boiling by-products. Cool to room

temperature, pour directly into the drain pipe (running water from the tap simultaneously), and wash the flask thoroughly with water, and finally with a little alcohol.

In the distillate, separate the upper layer of *n*-butyl cyanide and wash it with an equal volume of strong calcium chloride solution (40–50 per cent). Separate carefully and wash with 25–30 cc. of water, then with an equal volume of cold 50 per cent sulfuric acid [made by adding 40 g. (22 cc.) of concd. sulfuric acid to 40 cc. of cold water], and finally with about 50 cc. of a saturated sodium bicarbonate solution. Separate carefully, transfer the crude *n*-butyl cyanide to a small dry flask, and dry with about 5–10 g. of anhydrous calcium chloride. Through a funnel containing a small plug of cotton or glass wool, decant the dried liquid into a small distilling flask. Add a few small chips of clay plate and distil on an asbestos-centered wire-gauze. Collect in a dry, weighed bottle the portion boiling at 136–141°. The yield is 35–40 g. If a considerable amount of low-boiling product is obtained (b.p. 120–136°), dry this again with about 5 g. of anhydrous calcium chloride and refractionate.

➔ **Caution:** Sodium cyanide is extremely poisonous and must be manipulated with the greatest possible care. Always wash the hands thoroughly after manipulating it. Do not handle sodium cyanide if you have an open cut on your hand. Take great care not to acidify a solution containing sodium cyanide. Be sure to pour the residual cyanide solution directly into the drain pipe of the sink, and then turn on the water so that the solution is washed away completely into the drain pipe.

QUESTIONS

1. Write equations illustrating two methods of preparing *n*-butyl cyanide.
2. What is the structure of an isocyanide? How would you prepare *n*-butyl isocyanide?
3. Illustrate important differences in the reactions of cyanides and isocyanides which give evidence of the difference in their structures.

Experiment 54

PENTANOIC ACID (*n*-VALERIC ACID)

In a 500-cc. round-bottom flask, place 33 g. (41 cc.) of *n*-butyl cyanide, and add a solution of 30 g. of sodium hydroxide sticks in 100 cc. of water. Attach a long reflux condenser (60–70 cm. in length) and boil for four hours. Dilute the hot solution with 50 cc. of water and add cautiously through the condenser a warm solution of 46 g. (25 cc.) of concd. sulfuric acid in about 75 cc. of water. Shake vigorously, cool, and transfer to a 500-cc. separatory funnel. Rinse the flask with two 25-cc. portions of benzene and pour into the separatory funnel. Shake thoroughly and separate the benzene layer. Extract the aqueous layer with two or three 50-cc. portions of benzene. Transfer the combined benzene extracts to the separatory funnel and wash with 50 cc. of water. Dry with 8–10 g. of anhydrous magnesium sulfate or calcium sulfate (Drierite) and filter into a dry 500-cc. distilling flask. Remove the benzene and water by distilling on an asbestos-centered wire-gauze until the temperature of the vapors rises to 100°. Cool, transfer to a small distilling flask, and distil, using an air-cooled condenser. Collect in a dry, weighed bottle the pentanoic acid boiling at 180–186°. The yield is 24–28 g. Low-boiling material may be mixed with twice its volume of dry benzene, dried with 5–6 g. of anhydrous magnesium sulfate and redistilled.

n-Valeric acid may be characterized and identified by conversion to the crystalline anilide (or *p*-toluidide), using the same general procedure given for *n*-caproanilide (page 335).

QUESTIONS

1. What impurity is present in ordinary anhydrous calcium chloride which interferes with its use as a drying agent for pentanoic acid?
2. Show how one can obtain the following substances from *n*-butyl cyanide: pentanoic amide; ethyl pentanoate; *n*-pentyl amine.

Experiment 55

ETHYL *n*-BUTYLACETOACETATE

Alkylation of Acetoacetic Ester

Ethyl Sodio-Acetoacetate. In a perfectly dry 500-cc. round-bottom flask provided with a reflux condenser, place 150 cc. of high grade absolute alcohol.[1] In a small beaker containing kerosene or xylene weigh out 6.9 g. of clean metallic sodium. Through the condenser tube add the metallic sodium in small pieces, at such a rate that the alcohol is maintained in ebullition. After all the sodium has dissolved, add 39 g. (38 cc.) of pure ethyl acetoacetate to the warm solution of sodium ethylate (sodium ethoxide), with shaking. Proceed rapidly without interruption to the next step.

Ethyl *n*-Butylacetoacetate. To the clear solution of ethyl sodio-acetoacetate add 46 g. (36 cc.) of *pure* *n*-butyl bromide, and heat the reaction mixture on a steam-bath for six to ten hours. Place a calcium chloride tube at the top of the condenser to exclude atmospheric moisture. When the reaction is complete a drop of the solution will not show an alkaline reaction when tested with moist red litmus paper (Explain).

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[1] The grade of absolute alcohol used in this experiment is important since the yield of butylacetoacetic ester is decreased markedly by small amounts of water. Removal of the last traces of water from the alcohol may be accomplished by treatment with active quicklime, to obtain an absolute alcohol of 99.8 per cent purity. If the presence of methyl alcohol is not objectionable, a very anhydrous product may be obtained conveniently by the use of freshly prepared magnesium methylate as the drying agent. Since methyl alcohol is not objectionable in this experiment the magnesium methylate method is recommended here.

Provide a dry 1000-cc. round-bottom flask with a reflux condenser fitted with a calcium chloride tube, and place in the flask 2.4 g. of magnesium turnings and 20 cc. of absolute methyl alcohol. Usually a vigorous reaction occurs spontaneously and the magnesium dissolves. If necessary, warm the mixture gently or add a small crystal of iodine to start the reaction. When the magnesium has dissolved, a white paste of magnesium methylate results. Add 200 cc. of ordinary absolute ethyl alcohol (99–99.5 per cent) and reflux the mixture for four hours. Remove the reflux condenser and distil the absolute alcohol directly into the flask in which it is to be used, *taking precautions to protect the distillate from atmospheric moisture.* It is advisable to reject the first 15–20 cc. of distillate before collecting the main fraction.

Connect the flask by means of a wide delivery tube to a condenser set for distillation and distil off as much alcohol as possible by heating on a steam-bath. Cool the contents of the flask to 20° and add 250 cc. of water and 3 cc. of concd. hydrochloric acid. Transfer to a separatory funnel and draw off the aqueous layer of sodium bromide. Wash with a little water and dry with 8–10 g. of anhydrous magnesium sulfate. Transfer the liquid to a Claisen flask of suitable size and distil under diminished pressure.

Collect a first fraction which distils below 100° at 25 mm. pressure. This contains alcohol, water, *n*-butyl bromide, unchanged acetoacetic ester, and occasionally a trace of ethyl caproate (Explain). Collect the second fraction, which should consist chiefly of ethyl *n*-butylacetoacetate, from 120–130° at 25 mm. The yield is 32–38 g. A third fraction may be collected which on redistillation will yield a small additional quantity of ethyl *n*-butylacetoacetate. The residue in the distilling flask contains ethyl di-*n*-butylacetoacetate (b.p. 140–145° at 25 mm.).

To obtain perfectly pure ethyl *n*-butylacetoacetate it would be necessary to refractionate the main portion of the product and collect the material over a smaller boiling range. For the preparation of methyl *n*-amyl ketone further purification is unnecessary.

By treating an ethyl alkylacetoacetate with sodium ethoxide and an alkyl halide, a second alkyl group may be introduced with formation of an ethyl dialkylacetoacetate.

Alkylation and acylation will take place with most compounds containing an active methylene group similar to that in ethyl acetoacetate; however, the exact conditions of reaction differ. Acetylacetone ($CH_3COCH_2COCH_3$), for example, readily gives mono *C*-alkylation but attempted introduction of a second alkyl group frequently gives *O*-alkylation.

QUESTIONS

1. Explain what is meant by tautomerism and cite the experimental evidence for the existence of tautomeric forms of ethyl acetoacetate.
2. Point out the structural resemblance between phenol and the enol form of acetoacetic ester.
3. Write equations showing the mechanism of the formation of ethyl acetoacetate by the action of metallic sodium on ethyl acetate.
4. Write equations for the action of metallic sodium on the following: ethyl propionate; a mixture of ethyl benzoate and ethyl acetate; a mixture of acetone and ethyl acetate.

Experiment 56

METHYL *n*-AMYL KETONE (HEPTANONE-2)

Ketone Decomposition of a Substituted Acetoacetic Acid

Sodium *n*-Butylacetoacetate. In a 500-cc. separatory funnel (or bottle) place 250 cc. of 5 per cent sodium hydroxide solution and add the ethyl *n*-butylacetoacetate (32–38 g.) obtained in the preceding experiment. Stopper the container and shake thoroughly for about one-half hour. Allow the reaction mixture to stand at room temperature with occasional shaking for at least three to four hours (but not more than twenty hours). During this treatment the ethyl *n*-butylacetoacetate is saponified and passes into solution as the sodium salt of *n*-butylacetoacetic acid. A small oily layer of ethyl di-*n*-butylacetoacetate may remain undissolved; separate the aqueous solution of sodium *n*-butylacetoacetate from this layer before proceeding to the next step.

Methyl *n*-Amyl Ketone. Transfer the solution of sodium *n*-butylacetoacetate to a 1-l. flask provided with a cork fitted with a small separatory funnel and a wide delivery tube connected to an efficient condenser set for distillation. Through the separatory funnel add slowly with shaking, a cold solution of 15 cc. of concd. sulfuric acid in 30 cc. of water. During the addition of the acid a vigorous evolution of carbon dioxide occurs. When this has subsided heat the reaction mixture slowly to the boiling-point and distil slowly until 120–130 cc. of distillate has been collected. At this time the methyl *n*-amyl ketone should have distilled completely. The distillate contains the ketone, water, ethyl alcohol, and small amounts of acetic and caproic acids. Discard the residue.

To the distillate add small pieces of solid sodium hydroxide until the reaction is distinctly alkaline. Redistil the solution until 75–80 per cent of the material has passed over, and discard the residue. Separate the ketone layer in the distillate and redistil the aqueous layer until about one-third of the material has passed over. Separate the ketone layer and redistil the aqueous layer as before. Repeat this procedure as long as any appreciable amount of ketone is obtained in the distillate.

Wash the combined portions of the ketone four times with one-third its volume of 35–40 per cent calcium chloride solution. Dry over 4–5 g. of solid calcium chloride and distil. Collect the methyl *n*-amyl ketone from 146–152°. The yield is 10–15 g. If an appreciable low-boiling fraction is obtained it may be re-dried over calcium chloride and redistilled (or used for the preparation of the solid derivatives described below).

Semicarbazone of Methyl *n*-Amyl Ketone (Optional Experiment). This experiment illustrates the conversion of a ketone to a crystalline derivative suitable for identification and characterization.

Dissolve one gram of the ketone in 10 cc. of 60 per cent alcohol and pour this slowly, with shaking, into a solution of 1.2 g. of semicarbazide hydrochloride ($NH_2CONHNH_2,HCl$) and 1.8 g. of sodium acetate crystals in 15 cc. of water, contained in a small Erlenmeyer flask. Close the flask firmly with a softened cork and shake vigorously. The reaction takes place rapidly and white crystalline flocks of the semicarbazone soon fill the solution. Filter the crystals with suction, and wash with several small portions of cold water. Allow to dry and take the melting-point. The product may be purified by recrystallization from 60 per cent alcohol. The recorded m.p. of this semicarbazone is 127°.

2,4-Dinitrophenylhydrazone (Optional Experiment). In a 200-cc. round-bottom flask place 1 g. of methyl *n*-amyl ketone, 1 g. of 2,4-dinitrophenylhydrazine [$(NO_2)_2C_6H_3NHNH_2$] and 75 cc. of ethyl alcohol (95 per cent). Attach a reflux condenser and bring the mixture to the boiling-point. Extinguish the flame, allow the mixture to cool slightly, remove the condenser momentarily, and add 1.5 cc. of concd. hydrochloric acid (directly into the flask). The color changes to yellow-orange and the solution becomes clear. Adjust the condenser and boil gently for three to four minutes. Transfer the solution to an Erlenmeyer flask (filter through a fluted filter if the solution is not clear), close the flask loosely with a cork, and allow to cool slowly. If the solution is chilled rapidly the product may separate as an oil. Filter the crystals with suction, wash with a little cold alcohol, and recrystallize from ethyl alcohol. Take the melting-point. The recorded m.p. of this dinitrophenylhydrazone is 89°.

QUESTIONS

1. What side-reaction leads to the formation of acetic and caproic acids? How are they removed in the purification of the ketone?
2. How can methyl *n*-amyl ketone be prepared using a Grignard reaction?
3. How can methyl *sec*-butyl ketone (3-methylpentanone-2) be prepared by an acetoacetic ester synthesis?
4. How could methyl *n*-amyl ketone be regenerated from the semicarbazone or dinitrophenylhydrazone?

Experiment 57

ETHYL *n*-BUTYLMALONATE

Alkylation of Malonic Ester

Ethyl Sodio-Malonate. In a perfectly dry 1-l. round-bottom flask provided with a reflux condenser, place 250 cc. of high grade absolute alcohol.[1] In a small beaker containing kerosene or xylene weigh out 11.5 g. of clean metallic sodium. Through the condenser tube add the metallic sodium in small pieces, at such a rate that the alcohol is maintained in ebullition. After all the sodium has dissolved allow the sodium ethylate (sodium ethoxide) solution to cool slightly (to about 50°). To the warm solution add with shaking, 88 g. (80 cc.) of pure ethyl malonate during the course of five to ten minutes. Proceed rapidly without interruption to the next step.

Ethyl *n*-Butylmalonate. To the clear solution of ethyl sodiomalonate add gradually from a separatory funnel, 68.5 g. (54 cc.) of *pure n*-butyl bromide while shaking the flask to insure thorough mixing of the reactants. When the addition of the butyl bromide has been completed, add a few chips of clay plate and reflux the reaction mixture for four to five hours on a steam-bath. Place a calcium chloride tube at the top of the condenser to exclude atmospheric moisture.

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[1] The grade of absolute alcohol used in this experiment is important since the yield of butylmalonic ester is decreased considerably by small amounts of water. Removal of the last traces of water from the alcohol may be accomplished by treatment with active quicklime, to obtain an absolute alcohol of 99.8 per cent purity. If the presence of methyl alcohol is not objectionable, a very anhydrous product may be obtained conveniently by the use of freshly prepared magnesium methylate as the drying agent. Since methyl alcohol is not objectionable in this experiment the magnesium methylate method is recommended here.

Provide a dry 1000-cc. round-bottom flask with a reflux condenser fitted with a calcium chloride tube, and place in the flask 2.4 g. of magnesium turnings and 20 cc. of absolute methyl alcohol. Usually a vigorous reaction occurs spontaneously and the magnesium dissolves. If necessary, warm the mixture gently or add a small crystal of iodine to start the reaction. When the magnesium has dissolved, a white paste of magnesium methylate results. Add 300 cc. of ordinary absolute ethyl alcohol (99–99.5 per cent) and reflux the mixture for four hours. Remove the reflux condenser and distil the absolute alcohol directly into the flask in which it is to be used, *taking precautions to protect the distillate from atmospheric moisture.* It is advisable to reject the first 15–20 cc. of distillate before collecting the main fraction.

Connect the flask by means of a wide delivery tube to a condenser set for distillation and distil off as much alcohol as possible by heating on a steam-bath. Cool the contents of the flask to 20° and add 200 cc. of water and 5 cc. of concd. hydrochloric acid. Transfer to a separatory funnel and draw off the aqueous solution of sodium bromide. Wash the butylmalonic ester with a little water and dry with 10–15 g. of anhydrous magnesium sulfate. Transfer the liquid to a Claisen flask of suitable size and distil under diminished pressure.[1]

Collect first a low-boiling portion (alcohol, water, and *n*-butyl bromide) which distils below 100° at 25 mm. pressure. Collect next an intermediate fraction (unchanged malonic ester) up to 115° at 20–25 mm. pressure, and finally collect the main fraction of ethyl *n*-butylmalonate from 115–135° at 20–25 mm. pressure.[2] This weighs 65–75 g. If a large intermediate fraction is obtained this may be redistilled to secure an additional quantity of ethyl *n*-butylmalonate.

To obtain pure *n*-butylmalonic ester it would be necessary to refractionate the product but for many purposes (such as the preparation of *n*-caproic acid) further purification is unnecessary.

Ethyl malonate reacts similarly to ethyl acetoacetate (see page 321) in that two alkyl groups may be introduced in succession by repeating the procedure. Secondary alkyl derivatives are much more difficult to prepare, and tertiary alkyl derivatives cannot be prepared directly since the tertiary halides are converted to olefins under the conditions used.

QUESTIONS

1. Explain why the presence of water in any of the reagents used diminishes the yield of butylmalonic ester.
2. What is the precipitate which separates when ethyl sodio-malonate is treated with *n*-butyl bromide?
3. Can ethyl phenylmalonate be prepared by refluxing phenyl bromide (bromobenzene) with ethyl sodio-malonate?
4. Write equations for the preparation of ethyl malonate starting from acetic acid.
5. Write equations for the condensation of ethyl malonate with urea to form barbituric acid. Mention two derivatives of barbituric acid which are important synthetic drugs.

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[1] It is desirable but not essential to distil the product under diminished pressure; ethyl *n*-butylmalonate distils with only slight decomposition at 235–240° under 760 mm. pressure if the distillation is carried out rapidly from a small flask.

[2] Ethyl *n*-butylmalonate boils at 130–135° under 20 mm. pressure.

Experiment 58

n-CAPROIC ACID

Decarboxylation of a Substituted Malonic Acid

***n*-Butylmalonic Acid.** In this experiment use the entire quantity of ethyl *n*-butylmalonate obtained in the preceding preparation. In the first step use 1 g. of solid potassium hydroxide for each gram of ester, and in the subsequent acidification use 2 g. (1.1 cc.) of concd. sulfuric acid for each gram of potassium hydroxide.

In a 1-l. round-bottom flask place the solid potassium hydroxide and add an equal weight of distilled water. Shake thoroughly until the potassium hydroxide has dissolved completely. While shaking the flask vigorously add the *n*-butylmalonic ester dropwise to the hot solution, from a separatory funnel. Usually a vigorous reaction occurs and much of the alcohol formed boils off. During this process the flask should be held in a towel or clamp, and care must be taken to avoid spattering of the strong alkali upon the skin. To avoid this the ester must be added slowly and the flask shaken thoroughly.

After all of the ester has been added adjust a reflux condenser, add a few chips of clay plate, and boil the mixture for two or three hours to insure complete saponification. Remove the condenser, add about 150 cc. of water, and set the condenser for distillation. Distil the mixture until 130–140 cc. of distillate has been collected, to insure complete removal of alcohol. Discard the distillate.

Cool the reaction mixture to 20° and adjust a reflux condenser. Through the condenser tube add a *cold* solution of the requisite amount of concd. sulfuric acid (see above) dissolved in twice its volume of water. Perform this addition slowly with shaking in order to prevent excessive foaming. During the addition of the sulfuric acid the reaction mixture becomes warm and may reflux spontaneously. The solution now contains *n*-butylmalonic acid, potassium acid sulfate, and sulfuric acid.

***n*-Caproic Acid.** Add a few fresh chips of clay plate to the acid solution and reflux gently for four to six hours (longer refluxing may improve the yield slightly). Cool to 20°, separate the upper layer of organic acid, and extract the mother-liquor with three 150-cc. portions of benzene. Combine the original acid layer and

the benzene extracts, wash with 20–25 cc. of water, and dry with 10–15 g. of anhydrous magnesium sulfate.

Separate from the drying agent and distil off the benzene and last traces of water through a short fractionating tube, until the vapors reach a temperature of approximately 100°. Transfer the residue to a small distilling flask and distil carefully on a wire-gauze, using an air-cooled condenser. Collect the portion boiling from 198–206° in a dry, tared bottle. The yield is 20–25 g. Low boiling material may be dried again and redistilled.

If desired the final distillation may be carried out under diminished pressure, in a very small Claisen flask. The following are the boiling-points of *n*-caproic acid under diminished pressures: 99°/10 mm., 111°/20 mm., 119°/30 mm., 125°/40 mm., 130°/50 mm.

***n*-Caproanilide** (Optional Experiment). Organic acids are often identified and characterized by conversion to crystalline amides (anilides, *p*-toluidides, etc.) or to solid esters (*p*-nitrobenzyl, phenacyl esters, etc.). Anilides may be obtained conveniently by forming the acid chloride, using thionyl chloride, and treating with aniline.

In a large test-tube mix 1 g. of *n*-caproic acid with 2 g. (1.5 cc.) of *pure* thionyl chloride (sulfurous oxychloride, $SOCl_2$), attach a small reflux condenser, and boil gently for thirty minutes. After cooling, dissolve the liquid in 10 cc. of *dry* benzene, and pour slowly into a solution of 2 g. (2 cc.) of aniline in 20 cc. of *dry* benzene. Warm gently on a steam-bath for a few minutes to complete the reaction. Decant the benzene solution of the anilide into a separatory funnel, wash thoroughly with two 5-cc. portions of 5 per cent hydrochloric acid, then with 10 cc. of 5 per cent sodium hydroxide solution, and finally with pure water. Distil off the solvent from a small distilling flask and recrystallize the crude anilide from dil. alcohol, with addition of decolorizing charcoal. Dry thoroughly and take the melting-point.[1]

QUESTIONS

1. Why is the saponification of butylmalonic ester not necessarily complete when the oily layer of the ester has disappeared?
2. Why is it essential to remove all of the ethyl alcohol produced in the saponification before the solution is acidified?
3. Write complete equations for the preparation of the following acids by the malonic ester synthesis: 2-methylbutanoic acid; 3-phenylpropionic acid.
4. Why is malonic ester more satisfactory than acetoacetic ester in the synthesis of organic acids?

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[1] The reported melting-points of various anilides are: *n*-caproanilide, 95°; *iso*-caproanilide, 110°; *n*-valeranilide, 63°; *iso*-valeranilide, 109°; *n*-butyranilide, 92°; *iso*-butyranilide, 105°.

Experiment 59

FLUORESCEIN AND EOSIN

Fluorescein. Grind together in a mortar 10 g. of phthalic anhydride and 15 g. of resorcinol, and transfer the mixture to a 500-cc. round-bottom flask. Heat to 180° (internal temperature) in an oil-bath, and while stirring the mixture add in small portions 6 g. of pulverized fused zinc chloride. Precautions should be taken to avoid contact of the anhydrous zinc chloride with atmospheric moisture, by placing the pulverized solid in a specimen tube and adding small portions from the tube.

Continue to heat the mixture at 180° and stir the mass until it solidifies completely. The time required varies from forty-five minutes to one and one-half hours. Remove the flask, cool, and add 200 cc. of water and 10 cc. of concd. hydrochloric acid. Support the flask at an angle of about 45°, as in steam distillation, and pass water-free steam (through a trap, or from a laboratory generator; Fig. 14, Exp. 5) into the mixture for about thirty minutes, until the solid mass is loosened from the flask. With a glass rod, *carefully* complete the disintegration of the mass and filter with suction. Crush the crude product in a mortar, transfer to a suction filter, and wash thoroughly with water. Allow the product to dry in the air, or better in a drying oven at 80–100°. The yield of crude fluorescein is about 18 g.

The crude fluorescein is sufficiently pure for most purposes, and may be used directly for the preparation of eosin. Fluorescein may be purified by dissolving in warm alkalies and precipitation with acids, or better by conversion into the diacetate and hydrolysis of the pure diacetate.

Yellow and Red Forms of Fluorescein. Suspend 1 g. of pulverized fluorescein in 50 cc. of water and dissolve by adding 5 cc. of dil. sodium hydroxide solution (10 per cent). If necessary heat gently to hasten the solution. Filter the cold solution of the sodium salt and divide into two approximately equal portions.

Acidify one portion by adding 2–3 cc. of glacial acetic acid to the cold solution. Observe the color of the precipitated fluorescein.

Heat the second portion of the solution to boiling and add carefully 4–5 cc. of concd. hydrochloric acid diluted with an equal volume of water. Boil gently for a few minutes after all of the acid has been added. Observe the color of the precipitated fluorescein, and compare with the precipitate obtained by using acetic acid.

Fluorescein Diacetate. Place 2 g. of the pulverized, dry fluorescein in a small beaker and add 20 cc. (21 g.) of acetic anhydride and 1 cc. of concd. sulfuric acid. Warm the beaker *carefully* on an asbestos-centered wire-gauze with a small flame, until solution is complete. Filter the hot solution through a small fluted filter and cool the filtrate. Stir with a glass rod and allow the cold solution to stand for about thirty minutes to allow complete separation of the crystals of the diacetate. If the product does not crystallize readily from the solution, scratch the sides of the beaker with a glass rod or introduce a seed-crystal of the diacetate.

Filter the crystals with suction and wash with a little ether to remove the adhering mother-liquor. Crystallize from about 10 cc. of hot acetic anhydride, filter the purified fluorescein diacetate with suction, and wash with a small amount of ether. Allow the crystals to dry in the air. The yield is 1.0–1.2 g. of the purified product, which is practically colorless.

Eosin (Tetrabromofluorescein). In a 500-cc. round-bottom flask treat 10 g. of pulverized fluorescein with 40 cc. of glacial acetic acid, and add a solution of 24 g. (7.5 cc.) of bromine dissolved in 30 cc. of glacial acetic acid. Heat the mixture (preferably in a hood) on a steam-bath or in a bath of boiling water for one hour. The fluorescein dissolves as the soluble dibromo-derivative is formed, and finally a crystalline precipitate of the tetrabromo-derivative separates from the hot solution.

Pour the solution and the crystalline precipitate into 600–700 cc. of cold water to which 12–15 cc. of a saturated solution of sodium bisulfite has been added. Stir the mixture thoroughly and break up any lumps of the product. Filter with suction and wash the crude eosin thoroughly with water.

Suspend the crude eosin in 100 cc. of water and dissolve it as the sodium salt, by adding dil. sodium hydroxide solution (about 30–40 cc. of a 10 per cent solution is required). Pour the alkaline solution with stirring, into 600 cc. of boiling water containing 10–15 cc. of concd. hydrochloric acid, and boil the mixture for a few

minutes after all of the alkaline solution has been added. Cool and filter the purified eosin with suction. Wash thoroughly with water and allow to dry in the air. Eosin prepared in this way is a bright orange-colored powder. The yield is 16–18 g.

Sodium Salt of Eosin. In a mortar, grind thoroughly 6 g. of dry eosin and 1 g. of anhydrous sodium carbonate. Place the mixture in a 200-cc. beaker and moisten with 5 cc. of ethyl alcohol. Add exactly 5 cc. of water and warm gently on a steam-bath, with stirring, until the evolution of carbon dioxide ceases. Add 25 cc. of ethyl alcohol, heat to boiling, and filter the hot solution through a fluted filter. Upon cooling and allowing to stand, the sodium salt of eosin crystallizes from the solution in the form of green-red iridescent needles. The powdered crystals are dark red in color. The sodium salt sometimes separates very slowly from the solution; it is advantageous to cool and to scratch the sides of the beaker with a glass rod or to introduce a seed-crystal. Filter with suction and wash the crystals with a little ethyl alcohol. The yield is 4–5 g.

Ammonium Salt of Eosin. Over a small flat-bottom crystallizing dish, one-third filled with concd. aqueous ammonia, place a strong filter paper (preferably a hardened filter paper). Upon the filter paper place 3–4 g. of dry pulverized eosin, in a very thin layer. Cover the dish with a very large funnel and allow to stand for one or two hours, until the bright orange-colored eosin is converted completely into the dark red ammonium salt. The completeness of conversion may be tested by treating a small amount of the material with water; if the material dissolves entirely the conversion is complete.

QUESTIONS

1. Explain the color change which occurs when a phthalein, such as phenolphthalein or fluorescein, is treated with sodium hydroxide solution.
2. Explain the fact that fluorescein diacetate does not give a similar color change when treated with sodium hydroxide solution.
3. Write the structural formula for a sulfonephthalein, such as phenolsulfonephthalein or sulfonefluorescein, and indicate a method of preparation for such compounds.
4. Write equations showing a method of preparation for malachite green.
5. What is meant by the term, leuco-base? Write the structural formula of leuco-eosin (formed by the action of zinc dust on eosin in the presence of sodium hydroxide solution).

Experiment 60

HIPPURIC ACID

Synthesis in the Human Body

Hippuric acid is normally present in considerable quantities in the urine of herbivorous animals, but is present in very much smaller quantities in normal human urine. The average excretion of hippuric acid is about 0.7 g. per day for an adult man. Hippuric acid is formed in the body by synthesis from benzoic acid and glycine. Fruits (especially plums, prunes, and cranberries) increase the hippuric acid content of the urine on account of their relatively high content of benzoic acid. The output of hippuric acid is decreased in fevers and in certain kidney disorders where the synthetic activity of the kidneys is diminished.

In order to increase the amount of hippuric acid in the urine, so that it may be isolated conveniently, sodium or ammonium benzoate may be taken by mouth, either mixed with foodstuffs or in the form of an aqueous solution. The urine will then be found to contain much more hippuric acid than is normally present.

Ingestion of Benzoates. Before retiring at night, ingest 5 g. of pure sodium benzoate (or ammonium benzoate), by dissolving the solid in about half a glassful of water and taking the solution by mouth. Collect the overnight urine voided the next morning and isolate the hippuric acid as described below. The urine should be preserved from decomposition by adding about 10 cc. of toluene if the isolation of hippuric acid is not to be started within the next twelve hours. If toluene is used, it should be separated before proceeding to the next step.

Isolation of Hippuric Acid (Method of Roaf). Measure the volume of urine, and for every 100 cc. add 25 g. of pulverized solid ammonium sulfate and 1.5 cc. of concd. sulfuric acid. Stir thoroughly until the ammonium sulfate has dissolved, and set aside for several hours in a cool place or in an ice-bath, until the hippuric acid has separated as completely as possible. It is advantageous

to allow the solution to stand in a cool place overnight, since the hippuric acid separates slowly.

Filter the crystals with suction and wash with a little ice-water. Transfer the crystals to a beaker and purify by crystallization from about 50 cc. of hot water, with the addition of 1–2 g. of decolorizing charcoal. To aid in the removal of colored impurities it is advantageous to boil the hot solution for about ten minutes with the decolorizing charcoal before filtering the solution. Allow the filtrate to stand for at least an hour, and cool in an ice-bath before filtering the crystals of purified hippuric acid. Calculate the percentage yield of the hippuric acid isolated, assuming a complete conversion of the ingested benzoate into hippuric acid.

QUESTIONS

1. What is the source of the glycine which is used in the body in the synthesis of hippuric acid?
2. Suggest an explanation for the fact that benzoic acid is converted to hippuric acid in the body.
3. Compare in a general way, the synthetic processes which occur in animals, with the synthetic processes which occur in plants (especially the green plants).

Experiment 61

HIPPURIC ACID

The Schotten-Baumann Reaction

In a 1-l. round-bottom flask, place 270 g. (300 cc.) of concd. aqueous ammonia and add a solution of 25 g. of chloroacetic acid in about 25 cc. of water. Shake thoroughly during this addition and for a few minutes after all of the solution has been added. Cork the flask and allow to stand for at least twenty-four hours. The solution may stand longer without harm.

To this solution (which contains glycine, ammonium chloride, and excess ammonia) add a solution of 35 g. of sodium hydroxide in about 60 cc. of water. Transfer the solution to a large beaker, add a few chips of clay plate, and boil on an asbestos-centered wire-gauze (in a hood) until there is no longer any odor of ammonia. Cool to room temperature, transfer to a 250-cc. tincture-mouth bottle, and rinse the beaker with about 25 cc. of water. At this point the volume of the solution should be between 150–175 cc. If necessary, add water to bring the volume within this range.

Add 20 g. (17 cc.) of benzoyl chloride and stopper the bottle. Shake the mixture vigorously until the benzoyl chloride passes into solution. *Cautiously* release the internal pressure from time to time by carefully removing the stopper.

➔ **Caution:** The vapors of benzoyl chloride are very irritating to the eyes. The flask in which this material is stored should not be rinsed out into the sink until all traces of benzoyl chloride have been destroyed with a mixture of ammonia and alcohol.

When there is no longer any odor of benzoyl chloride (test cautiously), transfer the solution to a beaker and rinse the bottle with a small amount of water. If any precipitate is present in the alkaline solution, remove this by filtering with suction (discard the precipitate and save the solution). Precipitate the crude hippuric acid (contaminated with benzoic acid) by pouring the clear

alkaline solution with vigorous stirring *into* a mixture of 75 cc. of concd. hydrochloric acid and 75 g. of ice, contained in a large beaker. Cool if necessary, filter the crystals with suction, and press as dry as possible on the filter. Wash the crystals with about 25 cc. of cold water, and again press the crystals as dry as possible. To remove most of the benzoic acid, wash the crystals with several small portions of ether in the following way. Release the suction and loosen the crystalline cake with a porcelain spatula or a flattened glass rod. Add the ether in small amounts and stir into a paste. Continue to add small quantities of ether and mix the solvent thoroughly with the crystals. When a thorough mixing has been obtained, apply suction and press the crystals as free as possible from ether. Repeat this procedure two or three times. It is of great importance in washing crystals to stop the suction and to break up the crystalline cake so that the whole mass of crystals may actually come into contact with the washing liquid.

Crystallize the partly purified hippuric acid from hot water, with the addition of 1–2 g. of decolorizing charcoal, and allow the crystals to dry. The yield is 10–15 g. In determining the melting-point of hippuric acid it is advisable to use a bath of paraffin oil or di-*n*-butyl phthalate instead of cottonseed oil.

QUESTIONS

1. Explain why it is necessary to remove all of the ammonia before adding the benzoyl chloride.
2. Write an equation showing the action of the following reagents on hippuric acid: hot dil. hydrochloric acid; hot dil. sodium hydroxide solution.
3. Write an equation showing the action of benzoyl chloride, in the presence of aqueous sodium hydroxide, upon phenol; glycerol.
4. How is chloroacetic acid prepared?

Experiment 62

QUINOLINE

The Skraup Synthesis

In a 500-cc. flask fitted with a reflux condenser mix thoroughly (in the following order) 10 g. of finely powdered ferrous sulfate crystals ($FeSO_4$, $7H_2O$), 110 g. (88 cc.) of glycerol, 92 g. (50 cc.) of concd. sulfuric acid, 28 g. (28 cc.) of aniline, and 24 g. (20 cc.) of nitrobenzene. Heat gently over a wire-gauze until the mixture *begins* to boil, then remove the flame at once. The heat of reaction is sufficient to keep the mixture boiling steadily for about fifteen minutes. Should the reaction be too vigorous at the outset, supplement the reflux condenser by laying a wet cloth upon the upper portion of the flask. When boiling ceases replace the flame and heat the mixture to boiling for four hours longer. During this time arrange an apparatus for steam distillation, using a 2-l. round-bottom flask.

After allowing the reaction mixture to cool, dilute with an equal volume of water and pour it slowly into a funnel the tip of which is well under a solution of 100 g. of sodium hydroxide in 300 cc. of water, contained in the flask from the steam-distillation apparatus. Steam distil at once until no further oil passes over with the water (usually about 2 liters of distillate will be collected) and discard the reaction mixture in the flask. Separate the oily layer of crude quinoline in the distillate and extract the aqueous portion with three 50-cc. portions of benzene. Combine the benzene extracts and the crude quinoline, add 8 g. of *p*-toluenesulfonyl chloride, and warm for one-half hour on a steam-bath. Pour the mixture into 150 g. of ice and water and add concd. hydrochloric acid until an acid reaction to Congo-red test paper [1] is obtained. Usually about 20–30 cc. of acid will be required. Separate the aqueous layer by means of a separatory funnel and extract with two 25-cc. portions

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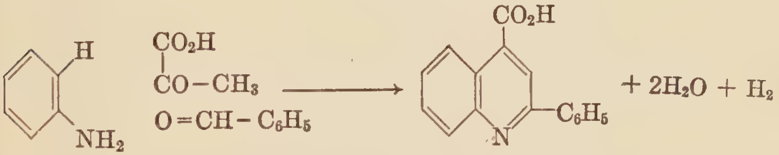
[1] Congo-red shows a *blue* color with mineral acids; it is not affected by weak acids or "acidic" salts. Quinoline hydrochloride shows an acid reaction to litmus but not to Congo-red.

of benzene. Save the aqueous layer and discard the benzene extracts.

Render the aqueous solution strongly alkaline by adding 40 per cent sodium hydroxide solution (prepared by dissolving 20 g. of sodium hydroxide in 30 cc. of distilled water), with stirring. Remove the quinoline by extracting the mixture twice with benzene, using 100 cc. for the first extraction and 50 cc. for the second. Dry the benzene extracts with 5–10 g. of anhydrous magnesium sulfate and distil off the benzene under ordinary pressure. Transfer the residual quinoline to a small Claisen flask and distil under diminished pressure; b.p. 110–115°/14 mm., 118–120°/20 mm., 132°/40 mm. The yield is 32–35 g.

The Skraup synthesis can be applied to a number of ring-substituted anilines (toluidines, anisidines, etc.) for the preparation of quinoline derivatives having substituents in the benzene ring. Thus, *p*-toluidine (with *p*-nitrotoluene instead of nitrobenzene) yields 6-methylquinoline, and *o*-toluidine (with *o*-nitrotoluene) gives 8-methylquinoline. If the nitro compound corresponding to the amine is not available, arsenic acid may be used as oxidizing agent in its place.

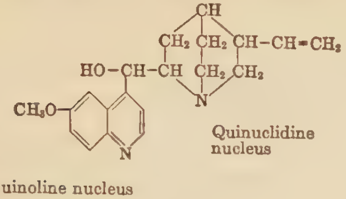
Cincophen is the trade name for 2-phenylquinoline-4-carboxylic acid, a synthetic drug which causes increased excretion of urine and is used widely in the treatment of gout. Cincophen is usually made by heating aniline, benzaldehyde, and pyruvic acid:



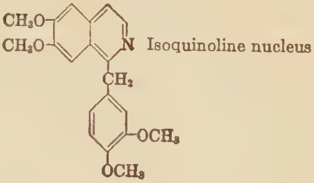
Quinoline derivatives with alkyl groups in the pyridine ring can be synthesized from aniline and various aliphatic compounds. Aniline and acetaldehyde on heating with hydrochloric acid yield quinaldine (2-methylquinoline). Quinoline, quinaldine, and lepidine (4-methylquinoline) react with alkyl halides to give quaternary ammonium salts which are starting materials for the preparation of an important class of dyes, the cyanine and isocyanine dyes. These are excellent sensitizers for the preparation of panchromatic photographic plates.

One of the most important medicinal alkaloids, quinine, so widely used in the treatment of malaria, is a quinoline derivative. Quinine and cinchonine are the principal alkaloids of a related group of natural bases occurring in the bark of the cinchona tree. The name quinoline was derived

from its relation to the quinine (cinchona) alkaloids. Another important group of alkaloids (*e.g.*, papaverine, from opium) contains the nucleus of isoquinoline, an isomer of quinoline in which the nitrogen atom of the pyridine ring is not directly attached to the benzene ring.



QUININE



PAPAVERINE

QUESTIONS

1. Write all of the steps involved in the Skraup synthesis and explain the function of the nitrobenzene and of the ferrous sulfate.

2. Explain the use of *p*-toluenesulfonyl chloride in removing unchanged aniline (cf. Exp. 36). Suggest another procedure for the removal of aniline from the crude quinoline.

3. How was the unchanged nitrobenzene removed from the crude quinoline?

4. What product would result if the Skraup synthesis were carried out using: β-naphthylamine? *o*-phenylene diamine (1,2-diaminobenzene)?

Experiment 63

ACETYLSALICYLIC ACID (ASPIRIN)

In a 50-cc. Erlenmeyer flask place 2 g. of pure salicylic acid. Add 5 cc. of acetic anhydride in such a way as to wash down any material adhering to the walls of the flask, and then 5 drops of syrupy (85 per cent) phosphoric acid. Heat the flask for five minutes on a steam-bath or in a beaker of water heated to 85–90°. Remove the flask from the bath, and, without allowing it to cool, add 2 cc. of water in one portion. The excess acetic anhydride decomposes vigorously and the contents of the flask come to a boil. (*Caution—Hot acid vapors!*)

When the decomposition is complete add 20 cc. of water and allow the flask to stand at room temperature until crystallization begins. The crystallization can be hastened by occasionally scratching the walls of the flask at the surface of the solution with a glass stirring rod. When crystals begin to appear place the flask in an ice-bath, add 10–15 cc. of cold water, and chill thoroughly until crystallization is complete. Collect the product on a Büchner funnel, suck as dry as possible, wash with cold water, and allow to dry thoroughly. The yield is 2.2–2.3 g.

Purify the crude product in the following way. In an Erlenmeyer flask (*not* a beaker) dissolve 1 g. of the *thoroughly dried* material in 10 cc. of ether by warming gently and stirring. To the solution (if not clear, filter into a clean flask) add 10 cc. of petroleum ether (b.p. 30–60°), stopper the flask, place in an ice-bath, and allow to cool undisturbed for about an hour. Collect the product on a Büchner funnel, wash with a little petroleum ether, and dry.

Dissolve a few milligrams of the pure product in about 1 cc. of methyl alcohol and add a drop of ferric chloride solution. Perform the same test on salicylic acid.

QUESTIONS

1. How is salicylic acid made commercially? How may salicylaldehyde be prepared?
2. What other derivatives of salicylic acid are used in medicine? Show how they may be prepared from salicylic acid.

Experiment 64

p-AMINOBENZENESULFONAMIDE (SULFANILAMIDE)

Sulfonation of Acetanilide with Chlorosulfonic Acid—Conversion of the Sulfonyl Chloride to the Sulfonamide—Selective Hydrolysis to the Aminoarylsulfonamide

p-Acetamidobenzenesulfonyl Chloride. In a *dry* 50-cc. Erlenmeyer flask place 36 g. (20 cc.) of chlorosulfonic acid [1] ($Cl—SO_3H$) (*handle carefully*—the acid causes severe burns if dropped on the skin). Cool the acid to 10–15°, but *not below 10°*, in a water-bath containing a few pieces of ice. Then add 7 g. of finely powdered, *dry* acetanilide, in small portions and with good mixing, so that the temperature does not rise above 20°. After the acetanilide has dissolved (a few small particles may remain undissolved), place the flask in a 600-cc. beaker containing just enough water to come about to the level of the reaction mixture in the flask. Heat the water to 60–70° and maintain this temperature for an hour. Take care that the water level is maintained during the heating so that the bath does not go dry; a large watch glass may be placed over the beaker to cut down evaporation.

Pour the reaction mixture *slowly and carefully* in a thin stream onto a well-stirred mixture of 150 g. of finely cracked ice and enough water to make stirring easy. *It is important to carry out this step cautiously to avoid spattering of the chlorosulfonic acid.* The reaction product separates as a white or pinkish-white gummy mass which soon becomes hard and can be broken up with a stirring rod. Break up any lumps which have formed, collect the

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[1] If a poor grade of chlorosulfonic acid is used the yield will be lowered. Discolored and impure specimens of the acid may be purified by distillation from an ordinary distilling flask (taking precautions to protect the distillate from moisture) provided the side-tube is passed as far as possible into the condenser to avoid contact of the vapor and distillate with corks. The distillation should be carried out fairly rapidly and not more than 50 cc. distilled in a single operation, since the corks are gradually attacked; rubber stoppers seem to be even less satisfactory than corks. If an all-glass distilling apparatus (with ground-glass joints) is available, this is ideal for the distillation. It is suitable to collect for use a fraction of chlorosulfonic acid boiling at 148–150° (760 mm.).

product on a Büchner funnel, and wash with several portions of cold water. The crude product, sucked as dry as possible, is used directly in the next step.[1]

***p*-Acetamidobenzenesulfonamide.** Place the crude, damp product from the first step in a 100-cc. Erlenmeyer flask and add 25 cc. of concd. aqueous ammonia (28 per cent). An immediate reaction ensues with the liberation of heat. Rub the mixture with a glass stirring rod until a smooth, thin paste is obtained and then heat at 70° for thirty minutes. Remove the flask to an ice-bath and after cooling add dil. sulfuric acid until the mixture is acid to Congo red. After thorough chilling in the ice-bath collect the product on a Büchner funnel, wash with cold water, and dry. The yield of crude product is 6–7 g. This material is sufficiently pure for the next step.

Recrystallize a small sample of the sulfonamide from hot water, using a little decolorizing charcoal (Norite or Darco) and take the melting-point of the purified material. Test the solubility of the product in dil. acid and dil. alkali. Explain the result.

The recorded melting-point for pure *p*-acetamidobenzenesulfonamide is 219°.

***p*-Aminobenzenesulfonamide.** Place the crude, dry *p*-acetamidobenzenesulfonamide obtained in the previous preparation in a 50-cc. Erlenmeyer flask and add an amount of dil. hydrochloric acid (1 volume of concd. acid to 2 volumes of water) equal to *two cc.* of dil. acid *per gram* of substance. Boil the mixture under reflux for one hour. Care should be taken at the start of the heating period to avoid charring of the initially pasty mixture.

Pour the solution into a 100-cc. Erlenmeyer flask and dilute with an equal volume of water. Add a little decolorizing charcoal (Norite or Darco), heat the solution to boiling, and filter through a fluted filter into a clean 600-cc. beaker. Add solid sodium carbonate in small portions with continuous stirring until the solution is just alkaline to litmus. During the neutralization the free amine separates as a white, crystalline precipitate. After thorough cooling in an ice-bath, collect the product by suction filtration, wash with

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[1] Moist *p*-acetamidobenzenesulfonyl chloride can be conveniently purified by dissolving in a mixture of acetone and benzene (1 : 1), separating the water, and allowing the solvent to evaporate until crystallization takes place. Obtained in this form the product keeps well, whereas the crude material even though dry cannot be preserved without considerable decomposition.

cold water, and dry. The yield is about 0.70–0.72 g. per gram of *p*-acetamidobenzenesulfonamide.

Recrystallize the product from water, using about 12 cc. of water per gram of sulfanilamide. Add a little Norite or Darco (about 0.5 g.) to the hot solution, boil for a few moments, and filter through a fluted filter paper in a short-stemmed funnel. The filter paper and funnel should be preheated by pouring boiling water through them just before filtering the solution, to prevent the material from crystallizing in the stem of the funnel. The sulfanilamide[1] separates on cooling as long, silky white needles. Test the solubility of sulfanilamide in dil. acid and dil. alkali. Explain the result.

The recorded melting-point of pure *p*-aminobenzenesulfonamide is 163°.

QUESTIONS

1. Compare the ease of hydrolysis of benzenesulfonamide and benzamide; of benzenesulfonyl chloride and benzoyl chloride. Compare the behavior of sodium benzenesulfonate and sodium benzoate on fusion with sodium hydroxide.

2. What is the formula for "sulfapyridine" (the new compound which is effective against "Type III" pneumococcus infections)?

3. What is saccharin? chloramine-T? How are they made commercially?

4. Why is it impractical to synthesize sulfanilamide by any process that would require *p*-aminobenzenesulfonyl chloride as an intermediate? What reaction would occur if *p*-aminobenzenesulfonyl chloride were formed momentarily in a synthetic process?

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[1] Sulfanilamide is a powerful therapeutic agent and must be taken only with the advice and supervision of a physician.

Experiment 65

FUMARIC ACID FROM FURFURAL

Oxidation with Vanadium Pentoxide Catalyst

Fit a 500-cc. Erlenmeyer flask with a two-hole cork bearing a reflux condenser and a small separatory funnel. In the flask place a solution of 45 g. of sodium chlorate ($NaClO_3$) in 100 cc. of water, add 0.2–0.3 g. of vanadium pentoxide catalyst,[1] and heat the flask to 70–75° in a water-bath. From a quantity of 20 g. (18 cc.) of furfural (a technical grade is satisfactory) measure 2–3 cc. and add this small portion to the oxidizing solution. Shake the flask and wait for the initial oxidation to occur before adding more furfural. The induction period varies from five to twenty minutes (occasionally longer).[2] From the separatory funnel add the remainder of the furfural *drop by drop*, in small quantities, with shaking after each addition. During the reaction the temperature of the solution rises to 100–105°. The rate of addition should be such that the vigorous reaction is maintained and all of the furfural is introduced in fifty to sixty minutes. If the aldehyde is added too rapidly the reaction becomes violent. It is important to insure that each portion of the aldehyde has reacted before adding the next. However, the oxidation must not be slowed down too much or the yield of fumaric acid is reduced.

After the addition of furfural is completed, heat the reaction mixture at 70–75° for three hours with occasional shaking, and then

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[1] Vanadium pentoxide can be purchased from Eimer and Amend (205 Third Avenue, New York), or from the Vanadium Corporation of America (120 Broadway, New York). The catalyst may be prepared from ammonium metavanadate (as described on page 367); it should be noted that this process requires several days' standing, and should be started in ample time ahead. The procedures for the oxidation and the preparation of the catalyst are essentially those of Milas (*Organic Syntheses*, Vol. 11, pages 46–47).

[2] It is essential *for safety* and for the success of the preparation to insure that the catalyst is active and that the first portion of furfural has reacted, before proceeding further. Occasionally specimens of vanadium pentoxide have little or no catalytic activity; if such material is encountered the experiment should be abandoned, since a sudden violent oxidation may occur if unreacted furfural is allowed to accumulate in the oxidizing mixture.

allow the mixture to stand overnight. Filter the crystalline fumaric acid with suction, wash sparingly with cold water, and press thoroughly on the filter. Recrystallize from hot water and allow the crystals to dry in the air. Do not attempt to determine the melting-point of fumaric acid unless special apparatus is available for high temperatures; fumaric acid melts in a sealed tube (to avoid sublimation) at 282–284°. The yield is 8–10 g.

A small additional amount of crude fumaric acid (1–2 g.) may be obtained by combining the mother-liquors from the oxidation and recrystallization, adding 5 cc. of concd. hydrochloric acid, concentrating on a steam-bath to a volume of about 70 cc., and cooling to 10–15°.

Preparation of Vanadium Pentoxide Catalyst. Suspend 1 g. of finely ground C.P. ammonium metavanadate [1] in 10 cc. of water and add slowly 1.5 cc. of concd. hydrochloric acid (sp. g. 1.18). Allow the reddish-brown, semi-colloidal precipitate to settle thoroughly (preferably overnight) and decant the supernatant solution. Add 10 cc. of water, shake thoroughly, and then allow to stand at room temperature for two or three days. This treatment renders the precipitate granular and easier to filter. Collect the precipitated vanadium oxide on a suction filter and wash several times with cold 5 per cent sodium chloride solution to remove hydrochloric acid. Do not wash with pure water or the oxide may become colloidal. Dry the product at 120° for twelve hours, grind to a fine powder, and dry again at 120° for twelve hours. The yield of catalyst is about 0.5 g., which is sufficient for two students.

QUESTIONS

1. How is furfural prepared commercially?

2. Does furfural resemble aliphatic or aromatic aldehydes in its general reactions? Cite several characteric reactions.

3. Write equations for two important commercial examples of vapor-phase oxidations using vanadium pentoxide catalyst.

4. Mention several other oxidation catalysts and the conditions under which they are used.

5. What type of isomerism is shown by maleic and fumaric acids? Cite experimental evidence used in establishing their configurations.

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[1] Ammonium metavanadate can be purchased from Eimer and Amend (205 Third Avenue, New York).

Experiment 66

POLYMERIZATION

Synthetic Polymers

Polymerization may be defined as the chemical combination of a number of identical or similar molecules to form a single molecule.[1] A polymer then will be any compound that can be formed by this process of multiple combination, or degraded by the reverse process (depolymerization).

Naturally occurring polymers of high molecular weight have for centuries played an important role in every day life—as foodstuffs (starches and proteins) and for providing shelter, fuel, clothing, and a variety of necessities and luxuries. A list of such polymers would include wood, cotton, paper, silk, wool, leather, rubber, lacquers and finishes, and a host of others. Chemical studies of native polymers have given a good working knowledge of their chemical constitution, and this information has served in two ways: (1) to enable modifications to be made in the properties of natural polymers by chemical transformations (rayon, celanese, cellophane, lacquers and finishes, photographic film, etc., from cellulose); (2) to lay the foundation for the synthesis of new polymeric materials from simple organic molecules. Examples of purely synthetic polymers are "Bakelite" resins from phenols and aldehydes, "alkyd" resins from glycols and dibasic organic acids, glass-like polymers ("butacite" and "lucite") from unsaturated esters, rubber-like polymers ("neoprene," "koroseal," "buna") from acetylene and other unsaturated compounds, and silk-like fibers ("nylon") and bristles ("exton") from diamines and dibasic organic acids.

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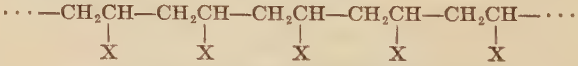
[1] Carothers, *Chemical Reviews*, 8, 355 (1931). General reference books in this field are: Ellis, *Chemistry of Synthetic Resins*, 2 vols., Reinhold Publishing Corp., New York, 1935; Morrell, *Synthetic Resins and Allied Plastics*, Oxford University Press, 1937; Burk, Thompson, Weith and Williams, *Polymerization and Its Applications in the Fields of Rubber, Synthetic Resins and Petroleum*, Reinhold Publishing Corp., New York, 1937.

Simple organic molecules can combine to form larger molecules either by direct addition, or by condensation reactions involving the elimination of water, ammonia, alcohol, etc. The formation of synthetic rubber from isoprene (and other 1,3-dienes) is a typical example of addition polymerization; the conversion of glucose to starches and cellulose, by intermolecular acetal formation with elimination of water, is an example of condensation polymerization. It will be seen that three different types of simple molecules can undergo polymerization: (1) compounds containing a reactive multiple bond ($C{=}C$, $C{\equiv}C$, $C{=}O$, etc.), (2) cyclic compounds, capable of undergoing ring-opening (alkylene oxides, lactones, lactams, etc.), (3) polyfunctional molecules (glycols, dibasic acids, hydroxy acids, etc.).

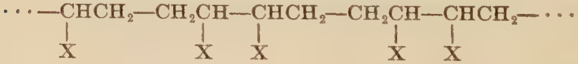
Addition Polymers. Self-combinations of this type can be illustrated by using the general formula $CH_2{=}CH{-}X$ to represent compounds such as vinyl acetate ($X = {-}O{-}CO{-}CH_3$), methyl acrylate ($X = {-}CO{-}OCH_3$), styrene ($X = {-}C_6H_5$), etc. The resulting polymeric molecules are long chains made up of a repeating series of identical structural units, each unit corresponding to one molecule of the starting material (called the monomer). Such linear polymers are usually mixtures containing chains of different lengths, and not a single pure individual. The terminal valences of the chain are saturated by univalent groups such as hydrogen, hydroxyl, acetoxyl, halogen, etc.

Three different types of polymeric structure may result from the self-combination of unsymmetrical compounds of the general formula $CH_2{=}CH{-}X$, depending upon the arrangement of the structural units in the chain:



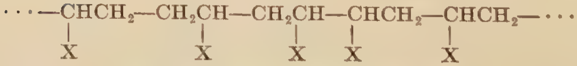
$$\cdots{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}\cdots$$

Type I (X groups in 1,3-positions)



$$\cdots{-}\underset{\underset{\displaystyle X}{|}}{CH}CH_2{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}\underset{\underset{\displaystyle X}{|}}{CH}CH_2{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}\underset{\underset{\displaystyle X}{|}}{CH}CH_2{-}\cdots$$

Type II (X groups in 1,2-positions)

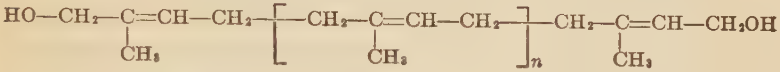


$$\cdots{-}\underset{\underset{\displaystyle X}{|}}{CH}CH_2{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}CH_2\underset{\underset{\displaystyle X}{|}}{CH}{-}\underset{\underset{\displaystyle X}{|}}{CH}CH_2{-}\underset{\underset{\displaystyle X}{|}}{CH}CH_2{-}\cdots$$

Type III (X groups in random positions)

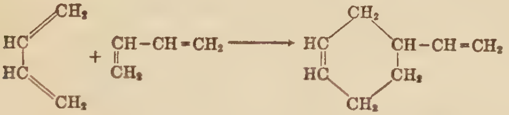
The structure of the linear polymer formed from a specific compound, under a particular set of conditions, can be formulated definitely only after an examination of its properties. The structure of commercial vinyl acetate polymer has been shown definitely to be Type I, but the constitution of many other polymers of this group is still in doubt.

Rubber-like polymers are formed from 1,3-dienes and their derivatives. In these dienes the presence of a conjugated system makes possible a 1,4-addition process. Natural rubber is a high molecular 1,4-polymer of 2-methyl-1,3-butadiene (isoprene) in which the terminal valences are satisfied by hydroxyl groups:



$$HO{-}CH_2{-}\underset{CH_3}{\underset{|}{C}}{=}CH{-}CH_2{-}\left[CH_2{-}\underset{CH_3}{\underset{|}{C}}{=}CH{-}CH_2{-}\right]_n{-}CH_2{-}\underset{CH_3}{\underset{|}{C}}{=}CH{-}CH_2OH$$

Rubber, like a number of other addition polymers, such as methyl methacrylate polymer ("Lucite") and polystyrene, can be degraded by destructive distillation at high temperatures into the parent monomer. Light, and organic peroxides, are active catalysts for the polymerization of vinyl compounds and of 1,3-dienes to long chain molecules. On heating in the presence of an antioxidant (hydroquinone, etc.), isoprene and 1,3-butadiene go mainly to cyclic dimers instead of rubbery polymers of high molecular weight.



Vinylcyclohexene, a cyclic dimer of 1,3-butadiene

It is of interest to note that an extensive group of natural products (camphor and other terpenes, carotene, lycopene, etc.) contain a carbon skeleton made up of isoprene units.

Examples of addition polymerization from cyclic monomers are the formation of polyethylene glycols from ethylene oxide, and the conversion of monomeric adipic anhydride to a linear polymer.

Condensation Polymers. Polyfunctional molecules (hydroxy acids, hydroxy aldehydes, glycols, dibasic acids, etc.) can react with themselves or with each other to give cyclic structures (especially 5- and 6-membered rings) or linear polymers.

The esterification of a polyhydric alcohol and a polybasic acid, with few exceptions, gives a mixture of long-chain polyesters of high molecular weight. A simple example of this type of reaction is afforded by the esterification of a bifunctional alcohol, ethylene glycol, with a bifunctional acid, succinic acid:

$$n\,\text{HO—(CH}_2\text{)}_2\text{—OH} + n\,\text{HO—CO—(CH}_2\text{)}_2\text{—CO—OH} \longrightarrow$$

$$\text{H—}\left[\text{—O—(CH}_2\text{)}_2\text{—O—CO—(CH}_2\text{)}_2\text{—CO—}\right]_n\text{—OH} + n\,\text{H}_2\text{O}$$

Linear polyester

Under conditions such that the water is removed very completely, there is obtained a product of high molecular weight (about 3000) which is built up by the combination of a large number of identical *structural units*, each containing an ester group. If an excess of the glycol is used the final product has two terminal alcohol groups; if the acid is used in excess the product has a free carboxyl group at the terminals:

$$\xrightarrow{\text{excess glycol}} \text{H—}\left[\text{—O—(CH}_2\text{)}_2\text{—O—CO—(CH}_2\text{)}_2\text{—CO—}\right]_n\text{—O—(CH}_2\text{)}_2\text{—OH}$$

$$\xrightarrow{\text{excess acid}} \text{HO—CO—(CH}_2\text{)}_2\text{—CO—}\left[\text{—O—(CH}_2\text{)}_2\text{—O—CO—(CH}_2\text{)}_2\text{—CO—}\right]_n\text{—OH}$$

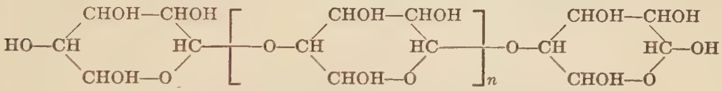
The physical and chemical characteristics of the polymeric material are influenced markedly by the degree of polymerization (number of structural units in the polymer) and the nature of the terminal groups. Polyesters containing a free hydroxyl and a free carboxyl group at the terminals can be obtained by intermolecular esterification of suitable hydroxy acids of the type $\text{HO—(CH}_2\text{)}_n\text{—CO}_2\text{H}$, where n is 5 or greater.

An important commercial example of polyesterification is the formation of synthetic resins and plastics ("alkyd" polymers) from phthalic anhydride and polyhydric alcohols, particularly glycerol. By controlling the relative amounts of the anhydride and alcohol, and the conditions of reaction, various polymers of different properties are obtained. A group of these has been given the name glyptals, derived from the words glycerol and phthalic. Under mild conditions (150°) only the primary alcohol groups are esterified and the secondary alcohol group remains free; the structural unit of the resulting polymers is the following:

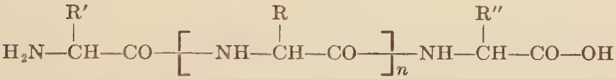
$$\text{——CO—C}_6\text{H}_4\text{—CO—O—CH}_2\text{—CHOH—CH}_2\text{—O——}$$

These are relatively soft materials and are soluble in a number of organic solvents. Under more drastic conditions (200–210°), and with a larger proportion of phthalic anhydride, the secondary alcohol groups are esterified and the simple chains become cross-linked, three-dimensional polymers of much higher molecular weight. These are relatively infusible, brittle materials that are insoluble in most solvents. In commercial practice the properties of the polymers are varied by mixing aliphatic acids or anhydrides with the phthalic anhydride. Like simple esters, the various polyesters can be saponified by alkalies to regenerate the parent acid and alcohol.

Other types of polymeric materials are polyacetals, from polyfunctional glycols and aldehydes, or from hydroxy aldehydes (*e.g.*, carbohydrates); polyamides, from polyfunctional acids and polyamines or from amino acids (*e.g.*, proteins, see page 171). In all of these the constitution of the polymer is represented as a long chain formed by combination of a large number of identical or similar structural units.



Polyacetal of Carbohydrate type, free alcohol at one terminal and free hemi-acetal group at the other. Simplified "Ideal" formula



$$H_2N-\overset{\overset{R'}{|}}{C}H-CO-\left[-NH-\overset{\overset{R}{|}}{C}H-CO-\right]_n-NH-\overset{\overset{R''}{|}}{C}H-CO-OH$$

Polyamide ("polypeptide") of Protein type, free amino at one terminal and free carboxyl group at the other Simplified "Ideal" formula

In the proteins the structural units are not all identical but are similar units derived from α-amino acids in which the individual R groups differ from each other. The simple formula represents an ideal case since some of the amino acid units in native proteins contain more than one amino or carboxyl group (lysine, arginine, aspartic acid, glutamic acid).

Condensation Polymers (Polyester Type)

Formation of a Glyptal Resin (Brittle Type). In a 200-cc. beaker place 10 g. of glycerol and 15 g. of pulverized, technical phthalic anhydride. Mix the materials thoroughly with a glass stirring rod and heat gently (150–175°) on an asbestos-centered wire-gauze over a small flame. Take care to avoid over-heating, which causes decomposition and charring of the product. As esterification proceeds water distils from the reaction mixture. Increase the heating gradually (200–210°) until the mass finally forms large bubbles which cause it to puff up to a large volume. At this point remove the flame and allow the polyester to cool. When cold, break up the brittle, clinker-like mass and remove it from the beaker as completely as possible. Pulverize the polymer in a mortar to obtain a fine powder.

Test the solubility of this polyester in the following solvents, using about 0.2 g. of polymer per 4–5 cc. of solvent and warming to the boiling-point (*caution with inflammable solvents*): acetone, carbon tetrachloride, toluene, ethyl alcohol, and any commercial solvents or plasticizers that may be available (cellosolves, carbitols, di-*n*-butyl phthalate, etc.).

A soft, soluble polyester may be obtained by heating one part by weight of glycerol with two parts of phthalic anhydride to 150–160° and discontinuing the heating when the first condensation is complete (see page 372).

Degradation of the polymer. In a small round-bottom flask place about 5 g. of the polyester and 25 cc. of dil. sodium hydroxide solution (10 per cent). Boil the mixture gently under reflux until the saponification is complete. What organic compounds are present in the solution? Outline a procedure for isolating and identifying them.

QUESTIONS

1. Write a structural formula for the polymer ("nylon") obtained from hexamethylene diamine [$NH_2(CH_2)_6NH_2$] and adipic acid [$CO_2H(CH_2)_4CO_2H$]. Indicate clearly the structural unit of the polymer.

2. Write formulas showing the structural units that would be formed by condensation of the following compounds: *n*-butyraldehyde and 1,5-pentanediol (polyacetal formation); succinaldehyde and the Grignard reagent from 1,5-dibromopentane (followed by treatment with dil. acid).

Addition Polymers (Vinyl Type)

Depolymerization by Heat. Place 20 g. of commercial granulated methyl methacrylate polymer ("Lucite") [1] in a small pyrex distilling flask provided with a tight cork and fitted to a condenser set for distillation. Heat the sides of the flask gently with a small luminous flame (3–4 cm.) which is rotated constantly.

The polymer gradually softens and at 300–325° undergoes rapid depolymerization to the monomer, methyl methacrylate,[1] which distils into the receiver. Continue the distillation *cautiously* until only a small black residue (3–4 g.) remains in the distilling flask. Place the distillate, amounting to 14–15 g., in a small flask and redistil; record the boiling range.

Polymerization. Place small samples of the monomer in three narrow test-tubes. To one add nothing, to another add a trace of hydroquinone (anti-oxidant), and to the third add a *very small* amount of catalyst (benzoyl peroxide). Make sure that no trace of hydroquinone is introduced into the third tube. *Cork the tubes firmly* and expose to sunlight for several days. Observe the physical change of the material from time to time.

QUESTIONS

1. Write equations showing how methacrylic acid [$CH_2{=}C(CH_3)CO_2H$] could be synthesized from acetone.
2. Write a possible structure for methyl methacrylate polymer.
3. Write equations, including the conditions of reaction, showing how ethylene oxide may be converted into: diethylene glycol, dioxane, methyl cellosolve, triethanol amine.
4. Write structural formulas for the terpenes, limonene and geraniol, and show how they may be derived from isoprene units.

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[1] Methyl methacrylate is the methyl ester of α-methyl acrylic acid (2-methylpropenoic acid). The granular form of the polymer is obtained by polymerizing the ester in an emulsified form; it may be purchased in small quantities from the Eastman Kodak Co. or in larger quantities from E. I. du Pont de Nemours and Co. Ammonia Department, Wilmington, Del. A similar polymer obtained from methyl acrylate is marketed by Röhm and Haas, Philadelphia, Pa. The latter, of course, gives methyl acrylate on degradation.

SUGGESTIONS FOR SUPPLEMENTARY EXPERIMENTS

It is desirable that certain standard laboratory manuals in organic chemistry be available for the benefit of students who are interested in organic syntheses and are qualified to perform supplementary experiments of an advanced type. The following are particularly useful: *Organic Syntheses*,[1] Collective Volume I (John Wiley and Sons, Inc., New York, 1932), and Gattermann-Wieland, *Laboratory Methods of Organic Chemistry* (English translation of the twenty-fourth German edition, by W. McCartney; The Macmillan Company, New York, 1937).[2]

Although the following list gives references to specific laboratory manuals, the student should be encouraged to consult comprehensive reference works [3] and original articles in the scientific journals.

In general the experiments listed below are comparable in scope to those in the last third of this manual, and an effort has been made to choose those illustrating important general reactions and typical laboratory operations. In a number of cases experiments are suggested in which preparations described in this manual serve as starting materials.

A few special notes are necessary in connection with the use of *Organic Syntheses*. The directions given there call for the use of relatively large quantities of materials and frequently for mechanical stirring. For a laboratory preparation the student will generally wish to use only one-fifth or one-tenth of the quantities mentioned. Care must be taken to decrease proportionately *all* of the reagents used. With smaller quantities the time required for various operations can usually be reduced considerably (but not proportionately) and stirring or shaking by hand will suffice if mechanical stirrers are not available.[1]

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[1] The individual volumes of *Organic Syntheses* are published annually—at present about twenty of these are available. Collective Volume I is a compilation and revision of preparations appearing in the first nine individual volumes; a cumulative subject index for volumes 10–19 is found in volume 19.

[2] Qualified students are encouraged to use the German edition of this work (*Die Praxis des organischen Chemikers*, Walter de Gruyter and Co., Berlin and Leipzig; obtainable from G. E. Stechert and Co., 31 East Tenth St., New York).

[3] For example: Houben-Weyl, *Die Methoden der organischen Chemie* (second and third edition, 4 volumes, 1921–1925, Verlag Georg Thieme, Leipzig).

In the following list the citations in *Organic Syntheses* refer to the Collective Volume I, except where an individual volume number is given. Others are Gattermann-Wieland, English translation of the twenty-fourth German edition (The Macmillan Co., New York, 1937); H. L. Fisher, *Laboratory Manual of Organic Chemistry*, fourth edition (John Wiley and Sons, Inc., New York, 1938); L. F. Fieser, *Experiments in Organic Chemistry* (D. C. Heath and Co., Boston, 1935).

BENZYL CYANIDE from benzyl chloride: Organic Syntheses, p. 101 (use one-twentieth quantities); Gattermann-Wieland, p. 137.

PHENYLACETIC ACID from benzyl cyanide: Organic Syntheses, p. 427 (use one-twentieth quantities); Gattermann-Wieland, p. 140.

BENZOPHENONE from *o*-benzoylbenzoic acid: L. F. Fieser, p. 199.

BENZOPINACOL and BENZOPINACOLONE from benzophenone: Organic Syntheses, **14,** pp. 8–13 (use one-tenth quantities); L. F. Fieser, p. 202.

BENZOHYDROL from benzophenone: Organic Syntheses, p. 84 (use one-tenth quantities).

p-TOLUYL-*o*-BENZOIC ACID from toluene and phthalic anhydride: Organic Syntheses, p. 503 (use one-fifth or one-tenth quantities).

β-METHYLANTHRAQUINONE from *p*-toluyl-*o*-benzoic acid: Organic Syntheses, p. 345 (use one-fifth or one-tenth quantities).

2,4-DIHYDROXYACETOPHENONE (RESACETOPHENONE) from resorcinol and acetonitrile (Exp. 21): Gattermann-Wieland, p. 347.

SALICYLALDEHYDE from phenol and chloroform: Gattermann-Wieland, p. 235.

CATECHOL from salicylaldehyde: Organic Syntheses, p. 143 (use one-tenth quantities).

MANDELIC ACID from benzaldehyde: Organic Syntheses, p. 329 (use one-tenth quantities); Gattermann-Wieland, p. 227; L. F. Fieser, p. 94.

d-MANDELIC ACID (resolution of racemic mandelic acid): Gattermann-Wieland, p. 228.

FURFURALACETONE from acetone and furfural: Organic Syntheses, p. 278 (use one-tenth or one-twentieth quantities).

FURAN from furoic acid (pyromucic acid): Organic Syntheses, p. 269 (use one-half or one-third quantities).

PYRROLE from mucic acid: Organic Syntheses, p. 461 (use one-fifth or one-tenth quantities).

NICOTINIC ACID (PYRIDINE-3-CARBOXYLIC ACID) from nicotine: Organic Syntheses, p. 378 (use one-tenth quantities).

DIBENZOYLMETHANE from benzalacetophenone (Exp. 46): Organic Syntheses, p. 199 (use about one-seventh quantities).

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[1] A simple and cheap mechanical stirrer, driven by compressed air, is described on page 383.

1,2-Diphenylethane (dibenzyl) from benzil (Exp. 47): Gattermann-Wieland, p. 383.

Mesitylene from acetone: Organic Syntheses, p. 334 (use one-tenth or one-twentieth quantities).

dl-α-Phenylethylamine from acetophenone (Exp. 33b): Organic Syntheses, **17**, p. 76 (use one-fifth or one-tenth quantities).

Resolution of *dl*-Phenylethylamine: Organic Syntheses, **17**, 80 (use all of material from preceding preparation).

Triphenylchloromethane from benzene and carbon tetrachloride: Gattermann-Wieland, p. 346.

Hexaphenylethane (triphenylmethyl) from triphenylchloromethane: Gattermann-Wieland, p. 352.

Iodobenzene from benzene, iodine, and nitric acid: Organic Syntheses, p. 316 (use one-tenth quantities); *cf.* Gattermann-Wieland, p. 283.

Phenyl iodochloride, iodosobenzene, and iodoxybenzene from iodobenzene: Gattermann-Wieland, p. 284.

Benzenesulfonyl chloride from sodium benzenesulfonate (Exp. 31a): Organic Syntheses, p. 77 (use one-tenth quantities); Gattermann-Wieland, p. 192.

m-Nitroaniline from *m*-dinitrobenzene: Gattermann-Wieland, p. 171 (use 35–40 g. of *m*-dinitrobenzene).

m-Nitrophenol from *m*-nitroaniline: Organic Syntheses, p. 396 (use one-tenth quantities).

Diphenic acid (diphenyl-2,2′-dicarboxylic acid) from anthranilic acid: Organic Syntheses, p. 216 (use one-fifth quantities).

β-Phenylhydroxylamine from nitrobenzene: Organic Syntheses, p. 436 (use one-tenth or one-twentieth quantities); Gattermann-Wieland, p. 174.

Nitrosophenylhydroxylamine and Cupferron from β-phenylhydroxylamine: Organic Syntheses, p. 171 (use one-twentieth quantities); Gattermann-Wieland, p. 177.

Quinone (1,4-benzoquinone) from hydroquinone: Organic Syntheses, p. 469 (use one-fifth or one-tenth quantities).

Quinone (1,4-benzoquinone) from aniline: Gattermann-Wieland, p. 309; L. F. Fieser, p. 228.

Isatin from aniline, chloralhydrate, and hydroxylamine: Organic Syntheses, p. 321 (use one-half or one-fourth quantities).

p-Nitrosodimethylaniline from dimethylaniline: Gattermann-Wieland, p. 316.

p-Aminodimethylaniline (dimethyl-*p*-phenylenediamine) from *p*-nitrosodimethylaniline: Gattermann-Wieland, p. 317.

Bindschedler's Green from *p*-aminodimethylaniline and dimethylaniline: Gattermann-Wieland, p. 321.

Malachite Green from benzaldehyde and dimethylaniline: Gattermann-Wieland, p. 324.

Martius Yellow and its reduction products, from α-naphthol: L. F. Fieser, p. 268.

COPPER PHTHALOCYANINE (MONOSTRAL BLUE) from phthalic anhydride: H. L. Fisher, p. 252.

TYRIAN PURPLE (6,6′-DIBROMOINDIGO) from *p*-toluidine: H. L. Fisher, p. 266.

DIMETHYLGLYOXIME from ethyl methyl ketone: H. L. Fisher, p. 191; for butyl nitrite see Organic Syntheses, **16**, p. 7.

DIPHENYLTHIOCARBAZONE (DITHIZONE) from phenylhydrazine: H. L. Fisher, p. 193.

PINACOL HYDRATE from acetone: Organic Syntheses, p. 448 (use one-fifth quantities); L. F. Fieser, p. 97.

PINACOLONE from pinacol hydrate: Organic Syntheses, p. 451 (use all of the pinacol hydrate obtained in the preceding preparation and carry out the reaction in a single operation); L. F. Fieser, p. 100.

METHYLAMINE from acetamide (Exp. 20): Gattermann-Wieland, p. 152.

NITROMETHANE from chloroacetic acid: Organic Syntheses, p. 393 (use one-fifth or one-tenth quantities).

NITROSTYRENE from benzaldehyde and nitromethane: Organic Syntheses, p. 405 (use one-twentieth quantities).

ADIPIC ACID from cyclohexanol: Organic Syntheses, p. 18 (use one-tenth or one-twentieth quantities).

METHYLETHYLACETIC ACID (α-METHYLBUTYRIC ACID) from *sec*-butyl chloride (Exp. 15c): Organic Syntheses, p. 353 (use entire quantities).

α-BROMO-*n*-CAPROIC ACID from caproic acid (Exp. 56): Organic Syntheses, p. 108 (use one-tenth quantities).

α-AMINO-*n*-CAPROIC ACID (*nor*-LEUCINE) from bromocaproic acid: Organic Syntheses, p. 40 (use all of the bromocaproic acid obtained in the preceding preparation).

ALANINE from acetaldehyde: Organic Syntheses, p. 20 (use one-tenth quantities); Gattermann-Wieland, p. 229.

dl-β-PHENYLALANINE from benzaldehyde and hippuric acid (Exp. 61): Organic Syntheses, **14**, p. 80; from benzaldehyde and acetylglycine, **19**, p. 67.

CAMPHOR from pinene (in five steps): H. L. Fisher, pp. 255–265.

ε-BENZOYLAMINOCAPROIC ACID from cyclohexanone oxime (Exp. 24): Organic Syntheses, **19**, p. 21 (use one-tenth quantities).

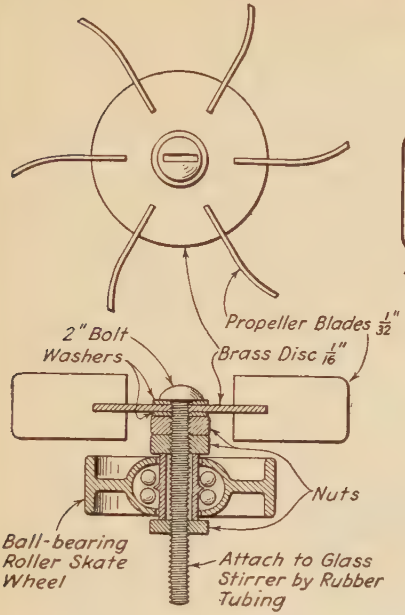
CYSTINE from human hair: Organic Syntheses, p. 188 (use one-tenth quantities).

GLUTAMIC ACID from wheat gluten: Organic Syntheses, p. 281 (use entire quantities given in directions).

TRIMYRISTIN from nutmegs: Organic Syntheses, p. 524 (use one-tenth quantities and carry out the extraction in an ordinary Soxhlet extractor [see p. 61 of this manual] of large size).

MYRISTIC ACID from trimyristin: Organic Syntheses, p. 371 (use all of the trimyristin obtained in the preceding preparation).

ARABINOSE from mesquite gum: Organic Syntheses, p. 60 (use one-fifth or one-tenth quantities).


2" Bolt
Washers
Propeller Blades $\frac{1}{32}$"
Brass Disc $\frac{1}{16}$"
Nuts
Ball-bearing Roller Skate Wheel
Attach to Glass Stirrer by Rubber Tubing

(One-half Actual Size)

FIG. 23.—Diagram of a Simple Air-driven Stirrer.

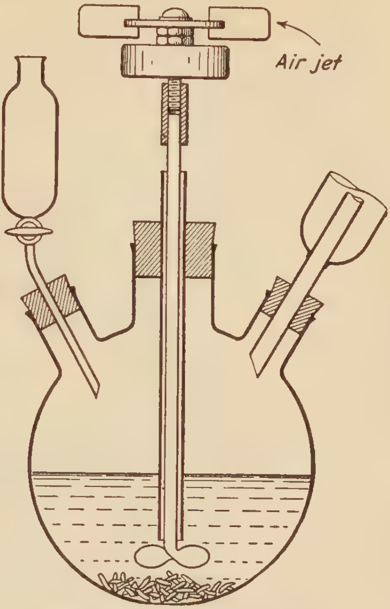


FIG. 24.—Typical Stirring Assembly.

This stirrer (suggested by Dr. W. T. Miller) can be constructed cheaply and easily from the following materials: a ball-bearing roller skate wheel (a pair of skates, costing about $1.25, furnishes eight of these); a disk of sheet brass $\frac{1}{16}$" thick and $1\frac{3}{4}$" diameter; six strips of sheet brass $\frac{1}{32}$" thick and measuring about $\frac{3}{4}$" × $1\frac{1}{4}$"; one 2" bolt with several nuts and washers. A hole $\frac{1}{4}$" in diameter is bored in the center of the brass disc and six slots ($\frac{1}{32}$") about $\frac{5}{16}$" long are cut at regular intervals into the outer edge. The six strips are fitted into the slots and soldered firmly in place. The blades are then curved as shown in the figure, and the outer corners bent slightly inward to afford better driving surface against the air jet. The bolt is inserted and the propeller is screwed tightly against the bushing of the ball-bearing. The lower, exposed end of the bolt is attached firmly to a glass stirrer by means of rubber tubing. The glass stirrer is held in a rather close-fitting sleeve of glass tubing. A typical stirring assembly, using a liquid-sealed stirrer in a three-necked flask, is shown in Fig. 24.

This stirrer stands up well in the laboratory and with 10–20 lb. air pressure is sufficiently powerful for ordinary stirring operations. With 25–30 lb. air pressure it is about equal to a small electric motor. If the lower air pressures are used it is helpful to insert eight propeller blades instead of six, or to use two air jets placed at opposite sides of the shaft. This type of stirrer is easily adjusted into position and is relatively free from vibrations; unfortunately it is rather noisy, especially with the higher air pressures.

Appendix

APPENDIX

APPROXIMATE TIME REQUIRED FOR EACH EXPERIMENT

(Time given does not include optional experiments)

Exp.	Arranging Apparatus *	Refluxing (R) or Standing (S) §	Working Time †	Exp.	Arranging Apparatus *	Refluxing (R) or Standing (S) §	Working Time †
1	½ hour	—	2–3 hours	31 c	—	5 hours(R)	1 hour
2	½ hour	—	1 hour	32 a	½ hour	½ hour(R)	1½–2 hours
3	½ hour	—	1–2 hours	32 b	—	½ hour(R)	1 hour
4	½ hour	—	3–4 hours	33 a	½ hour	1 hour(R)	3–4 hours
5	¼ hour	—	2–3 hours	33 b	½ hour	½ hour(R)	3 hours
6	—	—	1–2 hours	34	—	2 hours(R)	1–2 hours
7	½ hour	12 hours(S)	2 hours	35	½ hour	½ hour(R)	3–4 hours
8	—	—	2 hours	36	—	—	2 hours
9	—	—	½ hour	37	—	5–6 hours(R)	1 hour
10 a	½ hour	—	1 hour	38	—	—	1 hour
10 b	1 hour	—	3 hours	39	—	¾ hour(R)	1½ hours
11 a	¼ hour	—	2–3 hours	40	½ hour	—	3–4 hours
11 b	¼ hour	—	2–3 hours	41	—	—	2 hours
12	¼ hour	—	1 hour	42	—	3½ hours(R)	5 hours
13	½ hour	one week(S)	3 hours	43	—	—	5–6 hours
14	½ hour	12 hours(S)	2 hours	44	2 hours	—	2 hours
15 a	½ hour	2 hours(R)	3 hours	45	—	10 hours(S)	3 hours
15 b	½ hour	2 hours(R)	2 hours	46	—	2 hours(S)	1 hour
15 c **	½ hour	—	1½–2 hours	47	—	2 hours(R)	1½ hours
15 d	½ hour	12 hours(S)	2 hours	48 a	—	2 hours(S)	2 hours
16	¾ hour	—	3–4 hours	48 b	—	3 hours(R-S)	1 hour
17	½ hour	2 hours(R)	2 hours	49	—	3 hours(R)	1½ hours
18	—	—	2 hours	50	½ hour	4½ hours(R)	3 hours
19	½ hour	¾ hour(S-R)	1–1½ hours	51	—	4 hours(R)	3 hours
20	½ hour	5 hours(R)	2 hours	52	½ hour	¾ hour(R)	3 hours
21	½ hour	—	1 hour	53	¼ hour	30 hours(R)	4 hours
22 a	—	—	1 hour	54	¼ hour	4 hours(R)	2 hours
22 b	¼ hour	—	2 hours	55	1 hour	10 hours(R)	3 hours
23	½ hour	1 hour(S)	2–2½ hours	56	¾ hour	4 hours(S)	4 hours
24	—	12 hours(S)	1½–2 hours	57	1 hour	5 hours(R)	3–4 hours
25	—	—	1½–2 hours	58	1 hour	9 hours(R)	3–4 hours
26	—	—	2–3 hours	59	—	1½ hours(R)	4–5 hours
27	—	—	2 hours	60	—	12 hours(S)	1 hour
28	—	24 hours(S)	1–1½ hours	61	—	24 hours(S)	2 hours
29 a	—	5–6 hours(S)	4–5 hours	62	1 hour	4½ hours(R)	4–5 hours
29 b	—	3 hours(S)	4 hours	63	—	—	1–1½ hours
30	¾ hour	—	3–4 hours	64	½ hour	2½ hours(R-S)	2–2½ hours
31 a	—	—	1½–2 hours	65	½ hour	15 hours(S)	2 hours
31 b	—	—	1½–2 hours	66	½ hour	½ hour(R)	2–2½ hours

* The time given for arranging apparatus does not include any time for cleaning or drying glassware. The student should form the time-saving habit of cleaning his glassware immediately after use so that the desk equipment will be ready for use at all times.

§ In experiments where solutions are evaporated the time for this operation is listed under (S).

† The working time given in this table does not include time required for arranging apparatus.

** For *tert*-butyl chloride; if *sec*-butyl chloride is prepared as an alternative, two and one-half hours refluxing is required.

PHYSICAL PROPERTIES OF SOME ORGANIC SUBSTANCES

SUBSTANCE	M.P.	B.P. 760 MM.	SOLUBILITY			CRYSTAL FORM
			Water	Alcohol	Ether	
Acetone + sodium bisulfite $(CH_3)_2C(OH)—SO_2—ONa$	dec.		v. sol.	sl. sol.	insol.	leaflets/water
Benzenesulfonanilide $C_6H_5—SO_2—NHC_6H_5$	112°		sl. sol.	sol.	sol.	prisms/alc.
3-Bromo-4-acetamidotoluene $3—Br—4—CH_3CONH—C_6H_3CH_3$	117°		insol.	sol. hot	mod. sol.	needles
3-Bromo-4-aminotoluene $3—Br—4—NH_2—C_6H_3CH_3$	26°	240°	insol.	sol.	sol.	sp. g.^{20} 1.510
n-Butylacetoacetic acid $CH_3CO—CH(C_4H_9)—CO_2H$	dec.	dec.	v. sol.	sol.	sol.	decomposes spontaneously
n-Butyl isocyanide $CH_3—CH_2—CH_2—CH_2—NC$		118°	insol.	∞	∞	
n-Butylmalonic acid $C_4H_9—CH(CO_2H)_2$	102° dec.	dec.	80/100 at 50°	sol.	sol.	loses CO_2 on heating
n-Butylsulfuric acid $CH_3—CH_2—CH_2—CH_2—O—SO_2—OH$		dec.	v. sol.	sol.	sol.	syrup
n-Butyraldehyde + sodium bisulfite $CH_3—CH_2—CH_2—CHOH—SO_2—ONa$	dec.		v. sol.	sl. sol.	insol.	leaflets/water
o,p-Dibromoacetanilide *o,p*-$Br_2C_6H_3—NHCOCH_3$	146°		insol.	sl. sol.	sol.	needles
p,p'-Dibromodiphenylsulfone $(p\text{-}BrC_6H_4)_2SO_2$	172°		insol.	insol.		tablets/eth. acet.
Ethyl *n*-butylacetoacetate $CH_3CO—CH(C_4H_9)—CO_2C_2H_5$		dec.	insol.	sol.	sol.	sp. g.^{20} 0.97

PHYSICAL PROPERTIES OF SOME ORGANIC SUBSTANCES (*Continued*)

Substance	M.P.	B.P. 760 mm.	Solubility			Crystal Form
			Water	Alcohol	Ether	
Ethyl *n*-butylmalonate $C_4H_9\text{—}CH(CO_2C_2H_5)_2$		235°	insol.	sol.	sol.	sp. g.^{20} 0.96
Ethylsulfuric acid $C_2H_5\text{—}O\text{—}SO_2\text{—}OH$		dec.	v. sol.	sol.	sol.	syrup
Fluorescein diacetate $C_{20}H_{10}O_3(COCH_3)_2$	200°		insol.	sl. sol.	sl. sol.	needles
Furfural phenylhydrazone $C_4H_3O\text{—}CH{=}N\text{—}NHC_6H_5$	97°		insol.	sol.	sol.	
N-Methyl benzenesulfonanilide $C_6H_5\text{—}SO_2\text{—}N(CH_3)C_6H_5$	79°		sl. sol.	sol.	sol.	
Phenyl-α,β-dibromopropionic acid $C_6H_5\text{—}CHBr\text{—}CHBr\text{—}CO_2H$	200°	dec.	insol.	sol.	sol.	prisms
Phenyltrimethylammonium iodide $C_6H_5(CH_3)_3N\text{—}I$	228–29° dec.		sl. sol.	sl. sol.	insol.	leaflets
Sodium benzenesulfonate $C_6H_5\text{—}SO_2\text{—}ONa$	450° dec.		47/100	sl. sol. hot	insol.	needles + H_2O/alc.
Sodium *o*-bromobenzenesulfonate $o\text{-}BrC_6H_4\text{—}SO_2\text{—}ONa$	above 450°		sol.	sl. sol. hot	insol.	
Sodium *p*-bromobenzenesulfonate $p\text{-}BrC_6H_4\text{—}SO_2\text{—}ONa$	above 450°		sol.	sl. sol. hot	insol.	leaflets/alc.
p-Toluenesulfonanilide $p\text{-}CH_3\text{—}C_6H_4\text{—}SO_2\text{—}NHC_6H_5$	103°		insol.	sol.	mod. sol.	

DENSITY AND VAPOR PRESSURE OF WATER: 0° TO 35° C.

t,°C.	Vapor Pressure mm. Mercury	Density $d^{t^\circ}_{4^\circ}$	t,°C.	Vapor Pressure mm. Mercury	Density $d^{t^\circ}_{4^\circ}$	t,°C.	Vapor Pressure mm. Mercury	Density $d^{t^\circ}_{4^\circ}$
0°	4.58	0.99987	12°	10.48	0.99952	24°	22.18	0.99733
1°	4.92	0.99993	13°	11.19	0.99940	25°	23.54	0.99708
2°	5.29	0.99997	14°	11.94	0.99927	26°	24.99	0.99682
3°	5.68	0.99999	15°	12.73	0.99913	27°	26.50	0.99655
4°	6.09	1.00000	16°	13.56	0.99897	28°	28.10	0.99627
5°	6.53	0.99999	17°	14.45	0.99880	29°	29.78	0.99597
6°	7.00	0.99997	18°	15.38	0.99862	30°	31.55	0.99568
7°	7.49	0.99993	19°	16.37	0.99843	31°	33.42	0.99537
8°	8.02	0.99988	20°	17.41	0.99823	32°	35.37	0.99505
9°	8.58	0.99981	21°	18.50	0.99802	33°	37.43	0.99473
10°	9.18	0.99973	22°	19.66	0.99780	34°	39.59	0.99440
11°	9.81	0.99963	23°	20.88	0.99757	35°	41.85	0.99406

AQUEOUS ETHYL ALCOHOL

Density $d^{20^\circ}_{4^\circ}$	Per Cent C_2H_5OH by Weight	Per Cent C_2H_5OH by Volume	Grams C_2H_5OH per 100 cc.	Density $d^{20^\circ}_{4^\circ}$	Per Cent C_2H_5OH by Weight	Per Cent C_2H_5OH by Volume	Grams C_2H_5OH per 100 cc.
.98938	5	6.2	4.9	.85564	75	81.3	64.2
.98187	10	12.4	9.8	.84344	80	85.5	67.5
.97514	15	18.5	14.6	.83095	85	89.5	70.6
.96864	20	24.5	19.4	.81797	90	93.3	73.6
.96168	25	30.4	24.0	.81529	91	94.0	74.2
.95382	30	36.2	28.6	.81257	92	94.7	74.8
.94494	35	41.8	33.1	.80983	93	95.4	75.4
.93518	40	47.3	37.4	.80705	94	96.1	75.9
.92472	45	52.7	41.6	.80424	95	96.8	76.4
.91384	50	57.8	45.7	.80138	96	97.5	76.9
.90258	55	62.8	49.6	.79846	97	98.1	77.4
.89113	60	67.7	53.5	.79547	98	98.8	77.9
.87948	65	72.4	57.1	.79243	99	99.4	78.4
.86766	70	76.9	60.7	.78934	100	100	78.9

VAPOR PRESSURES OF ORGANIC SUBSTANCES AND OF WATER: 30° TO 120° C.

(In millimeters of mercury)

t, °C.	Water	Benzene	Bromo-benzene	*para*-Dibromo-benzene	*para*-Dichloro-benzene	Carbon Tetra-chloride	Toluene	Ethyl Alcohol
30	31.8	118	6	—	—	143	37	78
40	55.3	181	10	—	5	216	60	135
50	92.5	269	17	—	9	317	93	223
60	149.2	389	28	—	15	451	138	353
70	233.8	547	43	4	24	622	203	543
80	355.5	754	66	7	37	843	288	813
90	526.0	1016	98	12	56	1122	402	1187
100	760.0	1344	141	18	83	1463	557	1695
110	1074.	1748	199	28	119	1884	747	2364
120	1489.	2238	275	42	167	—	—	—

VAPOR PRESSURES OF ORGANIC SUBSTANCES AT 100° C.

(In millimeters of mercury)

Acetophenone	26.5	Dimethylaniline	37.9
Aniline	45.7	Diphenyl	9
Benzaldehyde	60.5	Ethyl benzene	307
Benzoic acid	1.8	Ethyl benzoate	17.4
Bromobenzene	141	Nitrobenzene	20.8
n-Butyl acetate	325	*p*-Nitrobenzoic acid	0.006
n-Butyl alcohol	390	*p*-Nitrotoluene	7.9
o-Chlorotoluene	133	Pentanoic acid	28.2
o-Cresol	13.6	Salicylic acid	0.86
p-Dibromobenzene	18	Toluene	557
p-Dichlorobenzene	83	Triphenyl carbinol	0.01

NOTE: The vapor pressures of salts, such as aniline hydrochloride and sodium acetate, are generally so low at 100° C., that they can be considered to be nil.

AQUEOUS HYDROCHLORIC ACID

Density $d^{15^{\circ}}_{4^{\circ}}$	Per Cent HCl by Weight	Grams HCl per 100 cc.	Density $d^{15^{\circ}}_{4^{\circ}}$	Per Cent HCl by Weight	Grams HCl per 100 cc.	Density $d^{15^{\circ}}_{4^{\circ}}$	Per Cent HCl by Weight	Grams HCl per 100 cc.
1.010	2.14	2.2	1.075	15.16	16.3	1.140	27.66	31.5
1.015	3.12	3.2	1.080	16.15	17.4	1.145	28.61	32.8
1.020	4.13	4.2	1.085	17.13	18.6	1.150	29.57	34.0
1.025	5.15	5.3	1.090	18.11	19.7	1.155	30.55	35.3
1.030	6.15	6.4	1.095	19.06	20.9	1.160	31.52	36.6
1.035	7.15	7.4	1.100	20.01	22.0	1.165	32.49	37.9
1.040	8.16	8.5	1.105	20.97	23.2	1.170	33.46	39.2
1.045	9.16	9.6	1.110	21.92	24.3	1.175	34.42	40.4
1.050	10.17	10.7	1.115	22.86	25.5	1.180	35.39	41.8
1.055	11.18	11.8	1.120	23.82	26.7	1.185	36.31	43.0
1.060	12.19	12.9	1.125	24.78	27.8	1.190	37.23	44.3
1.065	13.19	14.1	1.130	25.75	29.1	1.195	38.16	45.6
1.070	14.17	15.2	1.135	26.70	30.3	1.200	39.11	46.9

AQUEOUS NITRIC ACID

Per Cent HNO_3 by Weight	Density $d^{20^{\circ}}_{4^{\circ}}$	Grams HNO_3 per 100 cc.	Per Cent HNO_3 by Weight	Density $d^{20^{\circ}}_{4^{\circ}}$	Grams HNO_3 per 100 cc.	Per Cent HNO_3 by Weight	Density $d^{20^{\circ}}_{4^{\circ}}$	Grams HNO_3 per 100 cc.
5	1.0256	5.1	55	1.3393	73.7	91	1.4850	135.1
10	1.0543	10.5	60	1.3667	82.0	92	1.4873	136.8
15	1.0842	16.3	65	1.3913	90.4	93	1.4892	138.5
20	1.1150	22.3	70	1.4134	98.9	94	1.4912	140.2
25	1.1469	28.7	75	1.4337	107.5	95	1.4932	141.9
30	1.1800	35.4	80	1.4521	116.2	96	1.4952	143.5
35	1.2140	42.5	85	1.4686	124.8	97	1.4974	145.2
40	1.2463	49.9	90	1.4826	133.5	98	1.5008	147.1
45	1.2783	57.5	95	1.4932	141.9	99	1.5056	149.0
50	1.3100	65.5	100	1.5129	151.3	100	1.5129	151.3

AQUEOUS SULFURIC ACID

Per Cent H_2SO_4 by Weight	Density $d_{4°}^{20°}$	Grams H_2SO_4 per 100 cc.	Per Cent H_2SO_4 by Weight	Density $d_{4°}^{20°}$	Grams H_2SO_4 per 100 cc.	Per Cent H_2SO_4 by Weight	Density $d_{4°}^{20°}$	Grams H_2SO_4 per 100 cc.
5	1.0317	5.2	55	1.4453	79.5	91	1.8195	165.6
10	1.0661	10.7	60	1.4983	89.6	92	1.8240	167.8
15	1.1020	16.5	65	1.5533	101.0	93	1.8279	170.0
20	1.1394	22.8	70	1.6105	112.7	94	1.8312	172.1
25	1.1783	29.5	75	1.6692	125.2	95	1.8337	174.2
30	1.2185	36.6	80	1.7272	138.2	96	1.8355	176.3
35	1.2599	43.8	85	1.7786	151.2	97	1.8364	178.1
40	1.3028	52.1	90	1.8144	164.3	98	1.8361	179.9
45	1.3476	60.6	95	1.8337	174.2	99	1.8342	181.6
50	1.3951	69.6	100	1.8305	183.0	100	1.8305	183.0

Aqueous Sodium Hydroxide			Aqueous Ammonia			Fuming Sulfuric Acid		
Density $d_{4°}^{20°}$	Per Cent NaOH by Weight	Grams NaOH per 100 cc.	Density $d_{4°}^{20°}$	Per Cent NH_3 by Weight	Grams NH_3 per 100 cc.	Specific Gravity $d_{20°}^{20°}$	Per Cent Free SO_3 by Weight	Grams Free SO_3 per 100 cc.
1.0207	2	2.0	.9939	1	1.0	1.860	1.54	2.8
1.0428	4	4.2	.9895	2	2.0	1.865	2.66	5.0
1.0648	6	6.4	.9811	4	3.9	1.870	4.28	8.0
1.0869	8	8.7	.9730	6	5.8	1.875	5.44	10.2
1.1089	10	11.1	.9651	8	7.7	1.880	6.42	12.1
1.1309	12	13.6	.9575	10	9.6	1.885	7.29	13.7
1.1530	14	16.1	.9501	12	11.4	1.890	8.16	15.4
1.1751	16	18.8	.9430	14	13.2	1.895	9.43	17.7
1.1972	18	21.5	.9362	16	15.0	1.900	10.07	19.1
1.2191	20	24.4	.9295	18	16.8	1.905	10.56	20.1
1.2738	25	31.8	.9229	20	18.5	1.910	11.43	21.8
1.3279	30	39.8	.9164	22	20.2	1.915	13.33	25.5
1.3798	35	48.3	.9101	24	21.8	1.920	15.95	30.6
1.4300	40	57.2	.9040	26	23.5	1.925	18.67	35.9
1.4779	45	66.5	.8980	28	25.1	1.930	21.34	41.2
1.5253	50	76.3	.8920	30	26.8	1.935	25.65	49.6

Aqueous Acetic Acid			Aqueous Hydrobromic Acid			Aqueous Sodium Carbonate		
Per Cent CH_3-CO_2H by Weight	Density $d_{4°}^{20°}$	Grams CH_3-CO_2H per 100 cc.	Per Cent HBr by Weight	Density $d_{4°}^{20°}$	Grams HBr per 100 cc.	Per Cent $NaCO_3$ by Weight	Density $d_{4°}^{20°}$	Grams Na_2CO_3 per 100 cc.
10	1.0125	10.1	10	1.0723	10.7	2	1.0190	2.04
20	1.0263	20.5	20	1.1579	23.2	4	1.0398	4.16
30	1.0384	31.1	30	1.2580	37.7	6	1.0606	6.36
40	1.0488	42.0	35	1.3150	46.0	8	1.0816	8.65
50	1.0575	52.9	40	1.3772	56.1	10	1.1029	11.03
60	1.0642	63.8	45	1.4446	65.0	12	1.1244	13.50
70	1.0685	74.8	50	1.5173	75.8	14	1.1463	16.05
80	1.0700	85.6	55	1.5953	87.7	16	1.1682	18.50
90	1.0661	96.0	60	1.6787	100.7	18	1.1905	21.33
100	1.0498	105.0	65	1.7675	114.9	20	1.2132	24.26

ATOMIC WEIGHTS

Aluminum	Al	26.97	Manganese	Mn	54.93
Antimony	Sb	121.76	Mercury	Hg	200.61
Arsenic	As	74.93	Nickel	Ni	58.69
Barium	Ba	137.36	Nitrogen	N	14.01
Boron	B	10.82	Oxygen	O	16.00
Bromine	Br	79.92	Phosphorus	P	31.02
Calcium	Ca	40.08	Platinum	Pt	195.23
Carbon	C	12.00	Potassium	K	39.10
Chlorine	Cl	35.46	Silicon	Si	28.06
Chromium	Cr	52.01	Silver	Ag	107.88
Copper	Cu	63.57	Sodium	Na	23.00
Fluorine	F	19.00	Sulfur	S	32.06
Hydrogen	H	1.01	Tin	Sn	118.70
Iodine	I	126.92	Titanium	Ti	47.90
Iron	Fe	55.84	Vanadium	V	50.95
Magnesium	Mg	24.32	Zinc	Zn	65.38

OUTLINES OF VARIOUS LABORATORY COURSES

The order of the experiments and the number to be performed must be determined by the individual teacher to suit the needs of any particular class. The following outlines are intended to indicate the amount of work that may be expected, but no attempt has been made to select the "best" experiments. In a number of cases alternative experiments are given to illustrate a single type of reaction—this permits the teacher to make changes from year to year, while keeping to the same general outline. Particular attention is directed to the selection of sequences of preparations, of which a considerable number are offered in this manual, and to experiments involving test reactions. Sufficient experiments are included to permit students toward the end of the course to choose a few preparations according to their own interests.

Experiments 1, 2, and 3, on general laboratory procedures, will usually form a suitable introduction to the laboratory work for any group of students. Often it may be desirable to take up the other general procedures (fractional distillation, steam distillation, extraction, drying agents, etc.) as they are encountered from time to time in specific preparations.

For a one-semester course for students majoring in chemistry or chemical engineering, with six hours of laboratory work per week (including any necessary laboratory instruction by the teacher), the following list would be suitable: Experiments 1, 2, 3, 4, 9, 11 a or b, 14, 15 a b c or d, 17, 19, 20, 22 a, 22 b or 23, 24, 26, 27 and 28 (in part), 31 a b or c, 32 a or b, 35, 41, and 63. If a second semester of laboratory work is offered, the following are suggested: Experiments 33 a or b, 34, 36, 40, 42, 43, 44, 45, 46 or 48 or 50, 52, 55 and 56 or 57 and 58, 61 or 63 or 64, 62 or 65, and 66.

For a one-semester course for students in pre-medical, home economics, agricultural, and biological curricula, with six hours of laboratory work per week (including laboratory instruction by the teacher): Experiments 1, 2, 3, 4, 9, 11 a or b, 14, 18, 19 (reactions only), 20 (or 29 a or b), 22 a, 22 b or 23, 24, 26, 27, 31 a or c, 32 a, 35, 37 or 60, 41, and 63 or 64.

If only four hours a week are available for laboratory work the preceding list might be shortened by omitting experiments 4 (this operation is illustrated in Experiments 11 b and 20), 22 b and 23, 35 and two others, and by assigning only parts of some experiments.

For a short course with only three hours per week in the laboratory: Experiments 1, 2, 3, 9, 11 a (reactions only), 14 (A, B, C), 15 c (*tert*-Butyl chloride), 22 a, 24 (in part), 26 (in part), 36 (in part), and 63.

MATERIALS AND REAGENTS REQUIRED FOR THE EXPERIMENTS

The amounts listed below for each experiment are the quantities of materials and reagents needed for the use of ten students. Wherever an experiment specifies a variable quantity, the maximum amount has been taken. It is necessary in ordering materials to add to the quantities listed, on the average about 10 per cent, to take care of normal losses in handling and distributing. Ordinarily, repetition of experiments is sometimes required, which may increase the figures still more. Desk reagents [1] are included only when used in especially large amounts.

1. Determination of melting-points

Cinnamic acid	10 g.
Urea	10 g.
Cottonseed oil (*or* other bath liquid)	1 liter (920 g.)

2. Purification by crystallization

Impure acetanilide [2]	100 g.
Decolorizing charcoal (Norite)	20 g.
Impure naphthalene [3]	100 g.
Ethyl alcohol (95 per cent)	500 cc. (400 g.)
Decolorizing charcoal (Norite)	5 g.

3. Determination of boiling-points

Benzene	250 cc. (220 g.)
Benzene and toluene mixture (containing equal volumes of each	250 cc. (110 g. benzene, 110 g. toluene)

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[1] It will usually be found convenient to place the following reagents in the laboratory, so that they are available at all times: *Desk Reagents* (see page 7)—glacial acetic acid, hydrochloric acid (concd. and dil.), nitric acid (concd.), sulfuric acid (concd.), sodium hydroxide solution, ammonia; *Side-Shelf Reagents*—anhydrous calcium chloride, anhydrous magnesium sulfate, decolorizing charcoal, glycerol, anhydrous sodium carbonate and bicarbonate, sodium bicarbonate solution (saturated), sodium chloride (ordinary salt), stopcock grease, cotton.

[2] Satisfactory material for this purpose may be prepared by mixing thoroughly: 100 g. of ordinary acetanilide, 20 g. of ordinary sugar (sucrose), and 4–5 g. of sawdust that has been impregnated with 4–5 g. of aniline.

[3] Satisfactory material for this purpose may be prepared by mixing thoroughly: 100 g. of ordinary naphthalene, 5 g. of commercial biphenyl (or acetanilide), and 4–5 g. of sawdust.

4. Purification by fractional distillation

Carbon tetrachloride and toluene mixture (containing equal volumes of each)	1.2 liters (950 g. carbon tetrachloride, 520 g. toluene)
or benzene and toluene mixture	1.2 liters (530 g. benzene, 520 g. toluene)
or chloroform and toluene mixture	1.2 liters (900 g. chloroform, 520 g. toluene)
Asbestos paper (for wrapping columns)	

5. Steam distillation

Bromobenzene	200 cc. (300 g.)
p-Dichlorobenzene	50 g.
Salicylic acid	50 g.

6. Extraction with solvents

Glacial acetic acid	50 cc. (53 g.)
Ether	3.5 liters (2.5 kg.)
Normal sodium hydroxide solution	600 cc.

7. Salting-out effect. Drying agents

n-Butyl alcohol	600 cc. (515 g.)
Carbon tetrachloride	200 cc. (320 g.)
Quicklime (calcium oxide)	200 g.
Anhydrous calcium chloride	60 g.
Sodium chloride	100 g.

8. Qualitative detection of elements

Sugar (sucrose)	50 g.
Cupric oxide	20 g.
Quicklime (calcium oxide), halogen-free	60 g.
Copper wire	3 meters
Carbon tetrachloride	15 cc. (25 g.)
Sulfanilic acid	5 g.
Metallic sodium (under kerosene or xylene)	20 g.
Lead acetate solution (10 per cent)	10 cc.
Sodium nitroprusside solution (2 per cent)	10 cc.
Silver nitrate solution (5 per cent)	80 cc.
Lime water (saturated calcium hydroxide solution)	50 cc.
Barium chloride solution (10 per cent)	100 cc.
Ferrous sulfate solution (10 per cent)	10 cc.
Ferric chloride solution (10 per cent)	10 cc.
Asbestos paper	

9. Reactions of saturated hydrocarbons

Purified gasoline[1] (*or* petroleum ether, *or* ligroin)	120 cc. (90 g.)
Ordinary gasoline	120 cc. (90 g.)

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[1] Purified gasoline may be prepared from ordinary gasoline as described in the footnote of Exp. 9. A high grade of petroleum ether or ligroin may be used directly.

Paraffin oil[1]	120 cc. (100 g.)
Bromine water (saturated)	250 cc.
Potassium permanganate solution (0.5 per cent)	100 cc.
Sodium carbonate solution (10 per cent)	100 cc.

10a. Ethylene

Ethyl alcohol (95 per cent)	250 cc. (200 g.)
Concd. sulfuric acid	600 cc. (1.1 kg.)
Amorphous silica (kieselguhr, infusorial earth)	100 g.
Bromine water (saturated)	100 cc.
Potassium permanganate solution (0.5 per cent)	50 cc.
Sodium carbonate solution (10 per cent)	50 cc.

10b. Ethylene and ethylene dibromide

Bromine	150 cc. (480 g.)
Ethyl alcohol (95 per cent)	1.1 liters (900 g.)
Concd. sulfuric acid	1 liter (1.9 kg.)
Amorphous silica (kieselguhr, infusorial earth)	150 g.
Sodium bisulfite solution (saturated)	50 cc.
Anhydrous calcium chloride	60 g.
Sodium hydroxide solution (20 per cent)	600 cc.
Sodium bicarbonate solution (saturated)	300 cc.
Sodium chloride (ordinary salt)	1 kg.
Potassium permanganate solution (0.5 per cent)	50 cc.
Sodium carbonate solution (10 per cent)	50 cc.
Ice	

11a. Amylene (Pentene-2)

Pentanol-2 (*sec*-amyl alcohol)	360 cc. (300 g.)
Concd. sulfuric acid	350 cc. (650 g.)
Potassium permanganate solution (0.5 per cent)	30 cc.
Sodium carbonate solution (10 per cent)	30 cc.
Ice	
Bromine water (saturated)	30 cc.
Anhydrous calcium chloride	20 g.

11b. Cyclohexene

Cyclohexanol (technical or practical grade)	210 cc. (200 g.)
Anhydrous calcium chloride	40 g.
Sodium chloride (ordinary salt)	200 g.
Ice	
Bromine water (saturated)	30 cc.
Potassium permanganate solution (0.5 per cent)	30 cc.
Sodium carbonate solution (10 per cent)	30 cc.

12. Acetylene (Ethyne)

Calcium carbide	100 g.
Potassium permanganate solution (0.5 per cent)	50 cc.
Sodium carbonate solution (10 per cent)	50 cc.

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[1] Paraffin oil can be obtained from any central gasoline supply station in gallon quantities at a very reasonable price. It is also possible to use Nujol, Stanolind, etc.

Silver nitrate solution (5 per cent)	50 cc.
Ammoniacal cuprous chloride solution	100 cc.
or the following reagents:	
Copper sulfate crystals ($CuSO_4,5H_2O$)	35 g.
Sodium chloride	10 g.
Sodium bisulfite	10 g.

13. Ethyl alcohol (Ethanol)

Sucrose	800 g.
Pasteur's salts solution	700 cc.
Potassium phosphate	2 g.
Calcium phosphate	0.2 g.
Magnesium sulfate	0.2 g.
Ammonium tartrate	10 g.
Compressed yeast	5 cakes
Kerosene	75 cc. (60 g.)
Barium hydroxide solution (saturated)	100 cc.
Anhydrous potassium carbonate	200 g.
Iodine solution, in aqueous potassium iodide	100 cc.
Iodine	12.5 g.
Potassium iodide	25 g.
Glacial acetic acid	20 cc. (21 g.)

14. Test reactions of alcohols[1]

Iodine solution, in aqueous potassium iodide	250 cc.
Iodine	30 g.
Potassium iodide	60 g.
Glacial acetic acid	20 cc. (22 g.)
Metallic sodium (under kerosene or xylene)	5 g.
Methyl *or* ethyl alcohol (absolute)	50 cc.
Sodium dichromate solution (1 per cent)	50 cc.
Lucas' reagent (zinc chloride—hydrochloric acid)	350 cc.
Anhydrous zinc chloride (fused)	340 g.
Concd. hydrochloric acid	230 cc. (270 g.)
Alcohols for testing and for "unknowns"	
Ethyl alcohol (95 per cent)	60–80 cc.
n-Propyl alcohol	40–60 cc.
sec-Butyl alcohol	70–80 cc.
tert-Butyl alcohol	50–70 cc.
iso-Amyl alcohol	10–30 cc.
Additional alcohols[1] for testing and for "unknowns" *iso*-Propyl alcohol, *iso*-Butyl alcohol, *n*-Butyl alcohol, *n*-Amyl alcohol, *sec*-Amyl alcohols (pentanol-2 or pentanol-3), *tert*-Amyl alcohol.	15–25 cc. of each

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[1] The quantities of alcohols and reagents will vary according to the number of test reactions and of "unknowns" assigned to the class. The amounts listed will permit rather extensive testing. Technical or practical grades of alcohols may be used for the Lucas test provided the student is forewarned.

15a. *n*-Butyl bromide (1-Bromobutane)

Sulfur dioxide (from cylinder)	300 g.
Bromine	170 cc. (560 g.)
Ice	
n-Butyl alcohol	460 cc. (370 g.)
Sodium bisulfite solution (saturated)	50 cc.
Sodium bicarbonate solution (saturated)	300 cc.
Anhydrous calcium chloride	100 g.

15b. *n*-Butyl bromide (1-Bromobutane)

n-Butyl alcohol	460 cc. (370 g.)
Sodium bromide crystals ($NaBr,2H_2O$)	870 g.
Sodium bisulfite solution (saturated)	50 cc.
Sodium bicarbonate solution (saturated)	300 cc.
Anhydrous calcium chloride	100 g.

15c. *tert*-Butyl chloride (2-Chloro-2-methylpropane)

tert-Butyl alcohol (technical or practical grade)	350 cc. (280 g.)
Concd. hydrochloric acid	1250 cc. (1480 g.)
Sodium bicarbonate solution (5 per cent)	300 cc.
Anhydrous calcium chloride	60 g.

or

15c. *sec*-Butyl chloride (2-Chlorobutane)

sec-Butyl alcohol (technical or practical grade)	310 cc. (250 g.)
Anhydrous zinc chloride (fused)	900 g.
Concd. hydrochloric acid	550 cc. (630 g.)
Concd. sulfuric acid	250 cc. (460 g.)
Anhydrous calcium chloride	60 g.

15d. Ethyl iodide (Iodoethane)

Phosphorus (red)	25 g.
Ethyl alcohol (95 per cent)	300 cc. (240 g.)
Iodine	250 g.
Anhydrous calcium chloride	30 g.
Ice	

16. Diethyl ether

Ethyl alcohol (95 per cent)	1.5 liters (1.2 kg.)
Concd. sulfuric acid	500 cc. (920 g.)
Calcium chloride solution (40–50 per cent)	1 liter
Anhydrous calcium chloride	150 g.
Ice	

17. *n*-Butyl acetate

n-Butyl alcohol	230 cc. (185 g.)
Glacial acetic acid	180 cc. (190 g.)
Sodium carbonate solution (saturated)	500 cc.
Anhydrous magnesium sulfate [1]	60 g.

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[1] Anhydrous magnesium sulfate may be prepared readily by heating the crystalline hydrate, Epsom salts ($MgSO_4,7H_2O$), to dryness in a porcelain dish or casserole over a wire-gauze, and stirring with a porcelain spatula or glass rod until a dry powder is obtained. The loss in weight is about 50 per cent.

Sodium hydroxide (sticks)	100 g.
Sodium chloride	500 g.

18. Fats and fatty oils

Lard (*or* any fat *or* fatty oil)	130 g.
Sodium hydroxide (sticks)	75 g.
Ethyl alcohol (95 per cent)	500 cc. (400 g.)
Sodium chloride solution (saturated)	3 liters
Ivory soap (chips)	20 g.
Bromine solution, in carbon tetrachloride (2 per cent)	25 cc.
Calcium chloride solution (10 per cent)	10 cc.
Magnesium chloride solution (10 per cent)	10 cc.
Ferric chloride solution (10 per cent)	10 cc.
Potassium chloride solution (10 per cent)	10 cc.
Cottonseed oil (*or* linseed oil)	70 cc. (65 g.)
Linseed oil	70 cc. (65 g.)
Carbon tetrachloride	150 cc.
Litharge (lead monoxide)	10 g.

19. Acetyl chloride

Glacial acetic acid	230 cc. (240 g.)
Phosphorus trichloride	130 cc. (210 g.)
Aniline	10 cc. (10 g.)
Ethyl alcohol (95 per cent)	25 cc. (20 g.)
Sodium chloride solution (saturated)	20 cc.
Ice	

20. Acetamide

Ammonium acetate	500 g.
Glacial acetic acid	400 cc. (420 g.)
Benzene	30 cc. (26 g.)
Ethyl acetate	10 cc. (9 g.)
Yellow mercuric oxide	5 g.

21. Acetonitrile

Acetamide	200 g.
Phosphorus pentoxide	300 g.
Anhydrous potassium carbonate	250 g.

22a. Formaldehyde

Methyl alcohol	10 cc. (8 g.)
Copper wire	3 meters
Silver nitrate solution (5 per cent)	20 cc.
Formalin (40 per cent formaldehyde solution)	20 cc.
Ferric chloride solution (10 per cent)	10 cc.
Milk	50 cc. (0.1 pint)

22b. Acetaldehyde

Paraldehyde	200 cc. (200 g.)
Sulfamic acid *or* *p*-toluenesulfonic acid	20 g.

Silver nitrate solution (5 per cent)	20 cc.
Ammonia solution (2 per cent)	25 cc.
Fehling's solutions, No. 1 and No. 2	50 cc. of each
To prepare one liter of each of these solutions the following amounts of reagents are required:	
Copper sulfate crystals ($CuSO_4,5H_2O$)	35 g.
Sodium potassium tartrate (Rochelle salts)	170 g.
Sodium hydroxide (sticks)	50 g.
or Benedict's solution	100 cc.
To prepare one liter of this solution the following amounts of reagents are required:	
Sodium citrate	173 g.
Sodium carbonate, anhydrous	100 g.
Copper sulfate crystals ($CuSO_4,5H_2O$)	17 g.
Schiff's fuchsin-aldehyde reagent (0.5 g. *p*-rosaniline hydrochloride per liter)	10 cc.
Anhydrous calcium chloride	10 g.
Ice	

23. Cyclohexanone

Cyclohexanol (technical or practical grade)	210 cc. (200 g.)
Sodium dichromate crystals ($Na_2Cr_2O_7,2H_2O$)	420 g.
or Potassium dichromate ($K_2Cr_2O_7$)	410 g.
Concd. sulfuric acid	190 cc. (350 g.)
Sodium chloride (ordinary salt)	250 g.
Ether (ordinary)	200 cc. (150 g.)
Anhydrous magnesium sulfate	60 g.

24. Reactions of the carbonyl group in aldehydes and ketones[1]

(A) *n*-Butyraldehyde	50 cc. (40 g.)
Acetone	50 cc. (40 g.)
Ethyl alcohol (95 per cent)	500 cc. (400 g.)
Sodium bisulfite solution (saturated)	200 cc.
(B) Acetone	80 cc. (65 g.)
Hydroxylamine sulfate (*or* hydrochloride)	50 g.
Sodium hydroxide (sticks)	30 g.
or Cyclohexanone (from Exp. 23)	50 g. (53 cc.)
Hydroxylamine hydrochloride	50 g.
Sodium acetate crystals ($NaC_2H_3O_2,3H_2O$)	75 g.
Optional oxime test: furfural[1]	50 cc. (55 g.)
(C) *n*-Butyraldehyde	10 cc. (10 g.)
Semicarbazide hydrochloride	10 g.
Sodium acetate crystals ($NaC_2H_3O_2,3H_2O$)	15 g.
Optional semicarbazone tests: acetone, furfural, cyclohexanone (from Exp. 23), etc.[1]	

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[1] The quantities of aldehydes and ketones, and of reagents, will vary according to the number of test reactions assigned to the class. The amounts listed here cover

(D) Furfural	10 cc. (11 g.)
Cyclohexanone (from Exp. 23)	10 cc. (10 g.)
Phenylhydrazine hydrochloride [1]	20 g.
and Sodium acetate crystals ($NaC_2H_3O_2,3H_2O$)	30 g.
or Phenylhydrazine (base) [1]	20 cc. (22 g.)
Ice (for parts A, B, and C)	

25. Iodoform

Potassium iodide	125 g.
Acetone	30 cc. (25 g.)
Sodium hypochlorite (5 per cent solution) ("Clorox")	1.6 liters (4 lb.)
Anhydrous sodium carbonate	2 kg.
Ethyl alcohol (95 per cent)	500 cc. (400 g.)

26. Carbohydrates—sugars

Glucose	70 g.
Fructose	10 g.
Sucrose	10 g.
Lactose	10 g.
Maltose	10 g.
Fehling's solutions, No. 1 and No. 2	200 cc. of each
To prepare one liter of each of these solutions the following amounts of reagents are required:	
Copper sulfate crystals ($CuSO_4,5H_2O$)	35 g.
Sodium potassium tartrate (Rochelle salts)	170 g.
Sodium hydroxide (sticks)	50 g.
or Benedict's solution	400 cc.
To prepare one liter of this solution the following amounts of reagents are required:	
Sodium citrate	173 g.
Sodium carbonate, anhydrous	100 g.
Copper sulfate crystals ($CuSO_4,5H_2O$)	17 g.
Phenylhydrazine hydrochloride [1]	50 g.
and Sodium acetate crystals ($NaC_2H_3O_2,3H_2O$)	75 g.
or Phenylhydrazine (base) [1]	50 cc. (55 g.)
Sodium bisulfite solution	10 cc.
Fused sodium acetate	30 g.

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the specific examples given in the manual; if optional additional tests are to be done, larger quantities of the various reagents will be needed.

[1] Phenylhydrazine hydrochloride may be prepared from phenylhydrazine (base) by the following method: Dissolve 20 cc. (22 g.) of the base in 250 cc. of 95 per cent ethyl alcohol and add slowly, with shaking, a mixture of 25 cc. of concd. hydrochloric acid and 50 cc. of alcohol. Chill thoroughly and filter the hydrochloride with suction. Wash the crystals with two 20-cc. portions of cold alcohol, and finally with ether. The yield is 24–28 g. Note that phenylhydrazine (base) is poisonous and must be handled carefully.

Acetic anhydride	280 cc. (300 g.)
α-Naphthol (15 per cent solution in ethyl alcohol)	10 cc.

27. Carbohydrates—starches

Potatoes, raw	10
Cheese-cloth, and grater	
Starch	10 g.
Iodine solution, in aqueous potassium iodide	10 g.
Iodine	1 g.
Potassium iodide	2 g.
Fehling's solutions, No. 1 and No. 2	150 cc. of each
or Benedict's solution	300 cc.
For preparation of these see under Exp. 26.	
α-Naphthol (15 per cent solution in ethyl alcohol)	10 cc.

28. Carbohydrates—cellulose

Fehling's solutions, No. 1 and No. 2	50 cc. of each
or Benedict's solution	100 cc.
For preparation of these see under Exp. 26.	
Glacial acetic acid	200 cc. (200 g.)
Acetic anhydride	60 cc. (60 g.)
Absorbent cotton	15 g.
Chloroform	50 cc. (75 g.)
Ethyl alcohol (absolute)	150 cc. (120 g.)
Ether	150 cc. (110 g.)
Ethyl acetate	50 cc. (45 g.)

29a. Urea nitrate and urea

Urine	5 liters
Ethyl alcohol (95 per cent)	2.5 liters (2 kg.)
Potassium permanganate solution (0.5 per cent)	25 cc.
Decolorizing charcoal (Norite)	75 g.
Sodium hypochlorite solution (10 per cent)	10 cc.
Sodium nitrite solution (10 per cent)	10 cc.
Barium carbonate	120 g.

29b. Wöhler's synthesis of urea

Sodium hydroxide	125 g.
Sodium cyanide	125 g.
Potassium permanganate	268 g.
Sodium bisulfite	10 g.
Ammonium sulfate	500 g.
Methyl alcohol	700 cc. (560 g.)

30. Bromobenzene and *p*-dibromobenzene

Benzene	400 cc. (330 g.)
Iron wire (*or* tacks)	30 g.
or Anhydrous aluminum chloride	5 g.

Bromine	190 cc. (600 g.)
Ethyl alcohol (95 per cent)	1 liter (800 g.)
Anhydrous calcium chloride	60 g.

31a. Sodium benzenesulfonate

Benzene	230 cc. (200 g.)
Fuming sulfuric acid (7 per cent)	450 cc. (850 g.)
Sodium bicarbonate	250 g.
Sodium chloride	700 g.

31b. Sodium -bromobenzenesulfonate

Bromobenzene	110 cc. (160 g.)
Fuming sulfuric acid (7 per cent)	180 cc. (350 g.)
Sodium chloride	350 g.

31c. Sulfanilic acid

Aniline	140 cc. (140 g.)
Decolorizing charcoal (Norite)	30 g.
Concd. sulfuric acid	220 cc. (400 g.)

32a. Nitrobenzene

Benzene	270 cc. (235 g.)
Concd. nitric acid	250 cc. (350 g.)
Concd. sulfuric acid	300 cc. (550 g.)
Anhydrous calcium chloride	100 g.

32b. *p*-Bromonitrobenzene

Bromobenzene	105 cc. (160 g.)
Concd. nitric acid	190 cc. (280 g.)
Concd. sulfuric acid	200 cc. (370 g.)
Ethyl alcohol (95 per cent)	1.2 liters (1 kg.)

33a. Ethyl benzene

Ethyl bromide	330 cc. (440 g.)
Benzene	1.7 liters (1.5 kg.)
Anhydrous aluminum chloride	120 g.
Anhydrous calcium chloride	150 g.
Ice	

33b. Acetophenone

Acetic anhydride	240 cc. (260 g.)
Benzene, thiophene-free	1 liter (880 g.)
Anhydrous aluminum chloride	800 g.
Ether	500 cc. (360 g.)
Anhydrous calcium chloride	200 g.
Ice	

34. *p*-Nitrobenzoic acid

p-Nitrotoluene	230 g.
Sodium dichromate crystals ($Na_2Cr_2O_7,2H_2O$)	680 g.
Concd. sulfuric acid	920 cc. (1.7 kg.)

35. Aniline

Nitrobenzene	210 cc. (250 g.)
Tin, granulated	450 g.
Concd. hydrochloric acid	950 cc. (1.2 kg.)
Sodium hydroxide (sticks)	1.5 kg.
Ether	1.8 liters (1.3 kg.)
Sodium chloride	1 kg.

36. Reactions of primary, secondary, and tertiary amines

Acetic anhydride	93 cc. (100 g.)
Benzenesulfonyl chloride	42 cc. (30 g.)
Aniline	100 cc. (100 g.)
Methylaniline	100 cc. (100 g.)
Dimethylaniline	100 cc. (100 g.)
Methyl iodide	50 g.
Ethyl alcohol (70 per cent)	50 cc.
Samples of amines for identification (*e.g.*, pyridine, *o*-toluidine, *p*-toluidine, *m*-toluidine, *o*-anisidine)	
Medicine droppers, or graduated 1-cc. pipettes are desirable for this experiment	

37. Acetanilide

Aniline	200 cc. (200 g.)
Glacial acetic acid	240 cc. (250 g.)
Decolorizing charcoal (Norite)	30 g.

38. *p*-Bromoacetanilide

Acetanilide	135 g.
Glacial acetic acid	500 cc. (530 g.)
Bromine	53 cc. (170 g.)
Decolorizing charcoal (Norite)	30 g.
Ethyl alcohol (95 per cent	1.2 liters (960 g.)
Sodium bisulfite solution (saturated)	50 cc.

39. *p*-Bromoaniline

p-Bromoacetanilide (from Exp. 38)	100 g.
Ethyl alcohol (95 per cent)	200 cc. (160 g.)
Potassium hydroxide (sticks)	50 g.
Ice	

40. *o*-Chlorotoluene (*or* *p*-Chlorotoluene)

o-Toluidine (*or* *p*-Toluidine, 430 g.)	430 cc. (430 g.)
Concd. hydrochloric acid	1.4 liters (1.6 kg.)
Copper sulfate crystals ($CuSO_4,5H_2O$)	1.3 kg.
Sodium chloride	350 g.
Sodium bisulfite	270 g.
Sodium nitrite	280 g.
Sodium hydroxide (sticks)	180 g.

Anhydrous calcium chloride	50 g.
Ice	

41. Methyl orange (Helianthin)

Sulfanilic acid	110 g.
Sodium nitrite	35 g.
Dimethylaniline	63 cc. (60 g.)
Sodium carbonate solution (5 per cent)	600 cc.
Sodium hydroxide (sticks)	70 g.
Sodium chloride (ordinary salt)	200 g.

42. *m*-Bromotoluene

p-Toluidine	535 g.
Glacial acetic acid	1.6 liters (1.6 kg.)
Acetic anhydride	520 cc. (560 g.)
Bromine	270 cc. (820 g.)
Sodium bisulfite	70 g.
Ethyl alcohol (95 per cent)	4 liters (3.2 kg.)
Concd. hydrochloric acid	1.3 liters (1.6 kg.)
Sodium hydroxide (flakes *or* sticks)	350 g.
Concd. sulfuric acid	900 cc. (1.7 kg.)
Sodium nitrite	370 g.
Powdered copper (copper bronze)	90 g.
Sodium bicarbonate (satd. solution)	200 cc.
Anhydrous calcium chloride	30 g.
Starch-iodide test paper	
Ice	

43. Hydrazobenzene—benzidine—azobenzene

Nitrobenzene	250 cc. (300 g.)
Ethyl alcohol (95 per cent)	3.1 liters (2.5 kg.)
Sodium hydroxide (flakes *or* sticks)	150 g.
Zinc dust (good quality)	600 g.
Ether (ordinary)	2.1 liters (1.5 kg.)
Concd. hydrochloric acid	1 liter (1.2 kg.)
Sodium bisulfite solution	10 cc.
Bromine	32 cc. (100 g.)
Ice	

44. Distillation under diminished pressure

Benzaldehyde (technical or practical grade)	580 cc. (600 g.)
Sodium carbonate solution (10 per cent)	1 liter
Anhydrous magnesium sulfate	100 g.
Hydroquinone or catechol (anti-oxidant)	5 g.

or

Ethyl acetoacetate (technical or practical grade)	600 cc. (600 g.)
Sodium bicarbonate solution (saturated)	500 cc.
Anhydrous magnesium sulfate	100 g.
or Anhydrous potassium carbonate	100 g.

Ferric chloride solution (5 per cent)	20 cc.
Dilute aqueous solutions (1–2 per cent) of the following, for the enol tests: phenol, catechol, allyl alcohol, acetone.	

45. Benzyl alcohol and benzoic acid

Potassium hydroxide (sticks)	270 g.
Benzaldehyde (freshly distilled)	290 cc. (300 g.)
Ether (ordinary)	1.2 liters (870 g.)
Sodium bisulfite solution (saturated)	200 cc.
Sodium carbonate solution (10 per cent)	100 cc.
Anhydrous magnesium sulfate	50 g.
Concd. hydrochloric acid	750 cc. (900 g.)
Ice	

46. Benzalacetophenone

Acetophenone (freshly distilled)	120 cc. (120 g.)
Benzaldehyde (freshly distilled)	100 cc. (105 g.)
Ethyl alcohol (95 per cent)	1.4 liters (1.2 kg.)
Sodium hydroxide (sticks)	50 g.

47. Benzoin and benzil

Benzaldehyde (freshly distilled)	240 cc. (250 g.)
Ethyl alcohol (95 per cent)	500 cc. (400 g.)
Sodium cyanide (or potassium cyanide)	20 g.
Concd. nitric acid	400 cc. (580 g.)
Ice	

48a. Benzilic acid

Benzoin (from Exp. 47)	200–220 g.
Sodium hydroxide (sticks)	250 g.
Sodium bromate	60 g.
or Potassium bromate	65 g.
Concd. sulfuric acid	200 cc. (370 g).

48b. Benzilic acid

Benzil (recrystallized; from Exp. 47)	100 g.
Potassium hydroxide (sticks)	100 g.
Ethyl alcohol (95 per cent)	250 cc. (200 g.)
Benzene	540 cc. (480 g.)

49. Diphenylacetic acid

Benzilic acid (from Exp. 48a)	180 g.
Acetic acid (glacial)	500 cc. (525 g.)
Phosphorus, red	30 g.
Iodine	10 g.
Sodium bisulfite	50 g.
Ethyl alcohol (95 per cent)	1 liter (800 cc.)
Decolorizing charcoal (Norite)	20 g.

50. Cinnamic acid (*or* Furylacrylic acid)

Potassium acetate (freshly fused)	120 g.
or Sodium acetate (freshly fused)	100 g.
Acetic anhydride	280 cc. (300 g.)
Benzaldehyde (freshly distilled)	200 cc. (210 g.)
or Furfural (freshly distilled)	170 cc. (200 g.)
Decolorizing charcoal (Norite)	40 g.

51. β-Bromostyrene (1-Phenyl-2-bromoethylene)

Cinnamic acid (from Exp. 50)	150 g.
Carbon tetrachloride	2.1 liters (3.3 kg.)
Bromine	60 cc. (190 g.)
Ethyl alcohol (95 per cent)	1.2 liters (1 kg.)
Potassium acetate	300 g.
Sodium bicarbonate solution (saturated)	300 cc.
Anhydrous calcium chloride	50 g.
Ice	

52. Triphenyl carbinol

Magnesium turnings	24 g.
Ether (absolute)	1 liter (720 g.)
Bromobenzene	100 cc. (150 g.)
Ethyl benzoate	80 cc. (80 g.)
Ether (ordinary)	1 liter (720 g.)
Ethyl alcohol (95 per cent)	250 cc. (200 g.)

53. *n*-Butyl cyanide (*n*-Valeronitrile)

n-Butyl bromide (from Exp. 15a or b) [1]	700 cc. (890 g.)
Methyl alcohol	1.2 liters (960 g.)
Sodium cyanide	390 g.
Calcium chloride solution (40–50 per cent)	500 cc.
Sulfuric acid (50 per cent)	500 cc.
Sodium bicarbonate solution (saturated)	500 cc.
Anhydrous calcium chloride	100 g.

54. Pentanoic acid (*n*-Valeric acid)

n-Butyl cyanide (from Exp. 53)	410 cc. (330 g.)
Sodium hydroxide (sticks)	300 g.
Anhydrous magnesium sulfate	100 g.
Benzene	1.5 liters (1.3 kg.)

55. Ethyl *n*-butylacetoacetate

Absolute ethyl alcohol	2 liters (1.6 kg.)
Absolute methyl alcohol	200 cc. (160 g.)
Magnesium turnings	24 g.
Kerosene *or* xylene	250 cc.

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[1] If Exp. 53 is to be carried out a double quantity of butyl alcohol should be converted to the bromide in Exp. 15a or 15b, or accumulated student preparations of *n*-butyl bromide may be purified and used for Exp. 53.

Metallic sodium (clean)	69 g.
Ethyl acetoacetate (*pure*)	380 cc. (390 g.)
n-Butyl bromide (*pure;* from Exp. 15)	360 cc. (460 g.)
Anhydrous magnesium sulfate	100 g.
Ice	

56. Methyl *n*-amyl ketone (Heptanone-2)

Sodium hydroxide solution (5 per cent)	2.5 liters
Ethyl *n*-butylacetoacetate (from Exp. 55)	380 g.
Sodium hydroxide (sticks)	100 g.
Calcium chloride solution (35–40 per cent)	300 cc.
Anhydrous calcium chloride	50 g.
For optional preparations of derivatives:	
Semicarbazide hydrochloride	12 g.
Sodium acetate crystals ($NaC_2H_3O_2,3H_2O$)	18 g.
2,4-Dinitrophenylhydrazine	10 g.
Ethyl alcohol (95 per cent)	1 liter (800 g.)

57. Ethyl *n*-butylmalonate

Absolute ethyl alcohol	3 liters (2.4 kg.)
Absolute methyl alcohol	200 cc. (160 g.)
Magnesium turnings	24 g.
Kerosene *or* xylene	250 cc.
Metallic sodium (clean)	115 g.
Ethyl malonate (*pure*)	800 cc. (880 g.)
n-Butyl bromide (*pure;* from Exp. 15)	540 cc. (685 g.)
Anhydrous magnesium sulfate	150 g.

58. *n*-Caproic acid

Ethyl *n*-butylmalonate (from Exp. 57)	750 g.
Potassium hydroxide (sticks)	750 g.
Benzene	4.5 liters (4 kg.)
Anhydrous magnesium sulfate	150 g.
Ice	

59. Fluorescein and eosin

Phthalic anhydride	100 g.
Resorcinol	150 g.
Zinc chloride (fused)	60 g.
Acetic anhydride	300 cc. (315 g.)
Glacial acetic acid	700 cc. (745 g.)
Bromine	240 g. (75 cc.)
Sodium bisulfite solution (saturated)	150 cc.
Anhydrous sodium carbonate	10 g.
Ethyl alcohol (95 per cent)	300 cc. (240 g.)

60. Hippuric acid

Sodium benzoate	50 g.
Ammonium sulfate	2 kg.
Decolorizing charcoal (Norite)	20 g.

61. Hippuric acid

Chloroacetic acid	250 g.
Benzoyl chloride	170 cc. (200 g.)
Ammonia (concd.)	3 liters (2.7 kg.)
Sodium hydroxide (sticks)	350 g.
Ether	500 cc. (360 g.)
Decolorizing charcoal (Norite)	20 g.

62. Quinoline

Aniline	280 cc. (280 g.)
Nitrobenzene	200 cc. (240 g.)
Glycerol	880 cc. (1.1 kg.)
Concd. sulfuric acid	500 cc. (920 g.)
Ferrous sulfate crystals ($FeSO_4,7H_2O$)	100 g.
Sodium hydroxide (flakes *or* sticks)	1.2 kg.
p-Toluenesulfonyl chloride	80 g.
Benzene	2 liters (1.8 kg.)
Anhydrous magnesium sulfate	100 g.
Ice	

63. Aspirin

Salicylic acid	20 g.
Acetic anhydride	50 cc. (52 g.)
Phosphoric acid, syrupy (85 per cent)	5 cc.
Ether	100 cc. (75 g.)
Petroleum ether (b.p. 30–60°)	100 cc. (70 g.)
Methyl alcohol	10 cc.
Ferric chloride solution (5 per cent)	10 cc.

64. *p*-Aminobenzenesulfonamide (Sulfanilamide)

Acetanilide (dried thoroughly)	70 g.
Chlorosulfonic acid	200 cc. (360 g.)
Concd. aqueous ammonia	250 cc. (200 g.)
Decolorizing charcoal (Norite or Darco)	20 g.

65. Fumaric acid from furfural

Sodium chlorate	450 g.
Furfural	175 cc. (200 g.)
Vanadium pentoxide catalyst	3 g.
or Ammonium metavanadate, C.P.	6 g.

66. Polymerization

Glycerol	100 g.
Phthalic anhydride	150 g.
Solvents (acetone, carbon tetrachloride, toluene, ethyl alcohol; and others such as cellosolves, carbitols, dioxane, etc.)	50 cc. of each
Sodium hydroxide solution (10 per cent)	250 cc.
Granular methyl methacrylate polymer ("Lucite")	200 g.
Hydroquinone	1 g.
Benzoyl peroxide	1 g.

Treatment of Severe Burns

In Case of Accidents

TREATMENT OF SEVERE BURNS

Extensive burns, in which the burned area amounts to as much as 3 square feet, require special first aid to avoid a fatal outcome. *Summon medical aid at once.*

Large burns may be fatal as a result of the burn itself or of shock. Take precautions to avoid shock when giving first aid for any burn over 30–40 square inches in area. As soon as the fire is extinguished, carry or conduct the patient to a quiet room, lay him on a cot, and cover the unburned area with blankets. Keep the patient warm and quiet, and give water to drink. Expose the burned area and cut away any burned clothing. Pain may be relieved by spraying the burned area with 1 per cent aqueous solution of novocaine, with a little adrenaline added.

Further treatment should be carried on by a physician. For emergency treatment, if medical aid is not available within a half hour, a large burn may be covered with Crystal Violet jelly (1 per cent in a tragacanth jelly) [1] or with a similar preparation (such as tannic acid ointment made with some plasticizing agent) which forms a membrane over the burned area presumably fixing any toxic products produced by the burn, and by bacteriostatic action preventing low grade bacterial infection over a wide area. A fresh 5 per cent aqueous solution of tannic acid may be used instead of Crystal Violet jelly but is less desirable. With tannic acid solution the membrane formed, unless kept moist, becomes brittle and cracks, promoting infection and complications. About six weeks is normally required for a severe burn to heal completely. Crystal Violet stains can be removed by aromatic spirits of ammonia.

IN CASE OF ACCIDENTS

Always call or notify a laboratory instructor as soon as possible.

FIRE

Burning Reagents: Immediately extinguish any gas burners in the vicinity. Fire extinguishers are available in various parts of the laboratory. The newer type of extinguisher charged with carbon dioxide under pressure is usually more satisfactory than a liquid (carbon tetrachloride) extinguisher. If the latter is used, direct the liquid to the base of the flame. It is important to note that toxic vapors may be formed when carbon tetrachloride extinguishers are used, and are a source of danger in a confined space.

For burning oil use powdered solid sodium bicarbonate.

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[1] A suitable Crystal Violet jelly for use on burned areas is put on the market by the Calco Chemical Company.

Burning Clothing: Avoid running (which fans the flame) and take great care not to inhale the flame. Rolling on the floor is often the quickest and best method for extinguishing a fire on one's own clothing.

Smother the fire as quickly as possible using wet towels, laboratory coats, heavy (fire) blankets, or carbon dioxide extinguisher. *Do not use carbon tetrachloride (pyrene).*

Treatment of Small Burns: Do not wet the burned surface. Minor first or second degree burns in which an area not more than 2 square inches is reddened or blistered, but the skin not broken, may be treated with an anesthetic ointment such as butesin picrate ointment, or by borated vaseline and gauze bandage.

Small second or third degree burns in which blisters have formed and broken, or in which deep burns are encountered, should be freed carefully of all dead tissue *best by a physician* and dressed daily with borated vaseline bandages, with particular care to prevent infection.

Extensive Burns: These require special treatment to avoid a serious or fatal outcome—*summon medical aid at once.* Combat the effects of shock by keeping the patient warm and quiet, and giving water to drink. For emergency treatment see page 414.

INJURIES AND CHEMICAL BURNS

Reagents in the Eye: Wash immediately with a large amount of water; in the case of alkalies, follow with a saturated boric acid solution and, in the case of acids, follow with dilute sodium bicarbonate solution. Use an eye-cup to obtain thorough washing.

Reagents on the Skin: *Acids*—Wash with a large amount of water, then with dilute sodium bicarbonate solution, and finally with water. In the case of a serious wound, follow this treatment by applying a disinfectant, drying the skin, and covering with an ointment.

Alkalies—Wash with a large amount of water, then with very dilute acetic acid solution (1 per cent), and finally with water. In the case of a serious wound, follow this treatment by applying a disinfectant, drying the skin, and covering with an ointment.

Bromine—Apply glycerol (glycerine) immediately and liberally to the skin, and rub the glycerol into the pores. Remove the excess glycerol and apply an ointment such as butesin picrate or borated vaseline.

Organic Substances—Most organic substances can be removed from the skin by washing with ordinary alcohol, followed by washing with soap and warm water. If the skin is burned (as by phenol), apply an ointment such as butesin picrate or borated vaseline.

Cuts: Wash the wound with a disinfectant, and if necessary use a reagent from the first aid cabinet to stop the flow of blood.

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(Numbers in bold-faced type refer to pages on which methods of preparation are given.)

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IN CASE OF ACCIDENTS

Always call or notify a laboratory instructor as soon as possible.

FIRE

Burning Reagents: Immediately extinguish any gas burners in the vicinity. Fire extinguishers are available in various parts of the laboratory. The newer type of extinguisher charged with carbon dioxide under pressure is usually more satisfactory than a liquid (carbon tetrachloride) extinguisher. If the latter is used, direct the liquid to the base of the flame. It is important to note that toxic vapors may be formed when carbon tetrachloride extinguishers are used, and are a source of danger in a confined space.

For burning oil use powdered solid sodium bicarbonate.

Burning Clothing: Avoid running (which fans the flame) and take great care not to inhale the flame. Rolling on the floor is often the quickest and best method for extinguishing a fire on one's own clothing.

Smother the fire as quickly as possible using wet towels, laboratory coats, heavy (fire) blankets, or carbon dioxide extinguisher. *Do not use carbon tetrachloride (pyrene).*

Treatment of Small Burns: Do not wet the burned surface. Minor first or second degree burns in which an area not more than 2 square inches is reddened or blistered, but the skin not broken, may be treated with an anesthetic ointment such as butesin picrate ointment, or by borated vaseline and gauze bandage.

Small second or third degree burns in which blisters have formed and broken, or in which deep burns are encountered, should be freed carefully of all dead tissue *best by a physician* and dressed daily with borated vaseline bandages, with particular care to prevent infection.

Extensive Burns: These require special treatment to avoid a serious or fatal outcome—*summon medical aid at once.* Combat the effects of shock by keeping the patient warm and quiet, and giving water to drink. For emergency treatment see page 414.

INJURIES AND CHEMICAL BURNS

Reagents in the Eye: Wash immediately with a large amount of water; in the case of alkalies, follow with a saturated boric acid solution and, in the case of acids, follow with dilute sodium bicarbonate solution. Use an eye-cup to obtain thorough washing.

Reagents on the Skin: *Acids*—Wash with a large amount of water, then with dilute sodium bicarbonate solution, and finally with water. In the case of a serious wound, follow this treatment by applying a disinfectant, drying the skin, and covering with an ointment.

Alkalies—Wash with a large amount of water, then with very dilute acetic acid solution (1 per cent), and finally with water. In the case of a serious wound, follow this treatment by applying a disinfectant, drying the skin, and covering with an ointment.

Bromine—Apply glycerol (glycerine) immediately and liberally to the skin, and rub the glycerol into the pores. Remove the excess glycerol and apply an ointment such as butesin picrate or borated vaseline.

Organic Substances—Most organic substances can be removed from the skin by washing with ordinary alcohol, followed by washing with soap and warm water. If the skin is burned (as by phenol), apply an ointment such as butesin picrate or borated vaseline.

Cuts: Wash the wound with a disinfectant, and if necessary use a reagent from the first aid cabinet to stop the flow of blood.